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SOME NEWER ASPECTS OF URINARY SEDIMENT *

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In his remarkable paper entitled "The Lost Art of Urinalysis," A. S. Relman[1] said, . . . "at the present time, there is hardly a clinical procedure which is more neglected and to less advantage than the microscopic examination of the urine sediment. The medical students are not properly trained and the house officers avoid this 'dull chore.' The laboratory technicians are also rarely well trained and examine the sediment with a kind of resigned mechanical approach. . . . Therefore the usual examinations are worthless. . . . A cardiologist would not dream to let his EGG technician interpret the tracings; a hematologist would never depend upon a technician for interpretation of bone marrow. . . . Why does not the physician look at the urine? Is it because the urine, like feces, is an excretory product and is considered perhaps beneath the dignity of the physician? . . . In this age of radioactive tests, and electronic medical gadgetry, qualitative microscopic examination of the sediment probably does not have much romantic appeal. . . . Microscopic examination of the sediment is a job for the mature and medically trained observer, who is directly concerned with the care and treatment of the individual patient. . . ." We could not possibly think of better introductory words than these.

Although Richard Bright published his studies on renal disease a century and a half after the microscope was invented, he did not describe the urinary sediment. As a result, little could be done in classifying the various medical renal disorders which were then generally lumped together under the term "Bright's Disease." Recent years brought more precise daignostic techniques with more definite classification. Nevertheless the nosology of renal disease is still formative. Entities such as chronic pyelonephritis and acute tubular necrosis were clearly defined only within the past two decades.[1]

In the Middle Ages, uroscopy was considered as one of the most important diagnostic tools available. In the treatise "De Cautalis," attributed to Arnald of Villanova (1235?-1311), there is an extensive chapter dealing with patients who sometimes tested their doctor's skill and knowledge by sending the urine from other persons, animal urine or various juices.[2] These "water doctors" were probably over-enthusiastic about their uroscopies, but at least they correctly realized the significance of urinalysis. Even during Bright's life, the importance of urinary sediment was known. Vigla in France (1837) and later Rayer gave us the first descriptions of urinary casts.

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In 1846, Golding Bird regarded casts as pathognomonic of Bright's disease.[3] It was Thomas Addis who can be considered the founder of the modern school of interpretation of urinary sediment. In addition to numerous works on renal pathology and associated abnormalities in the urinary sediment, Addis rediscovered and properly understood the significance of the broad or renal failure casts:

"In spite of a wide, though necessarily incomplete and somewhat desultory search of the clinical literature of the last 25 years, I have failed to find any reference to the existence of broad casts. This is a remarkable circumstance, since no one who has looked at the fresh sediment from patients with uremia can have failed to see them. It is an index of the preoccupation of clinical investigators with functional methods to the exclusion of the morphology, and their quite unwarranted faith in the dictum of Schlanger and others to the effect that little or nothing can be learned from the microscopic examination of the urine. All the descriptions of these casts that I have found have dated from the period before the advent of methods of functional diagnosis."[4]

Thus wrote Addis thirty-five years ago and were he alive today, he would certainly be disappointed by the small number of physicians properly aware of the significance of broad casts, and urinary sediment.

Oval fat bodies, fatty casts and other fatty elements in the urinary sediment share a similar history. Though first described in 1913 by Munk in cases of lipoid nephrosis, the doubly refractile lipoid bodies fell into oblivion and neglect; they were mentioned only sporadically, mostly only in reference to experimental works and their significance was considered hardly more than academic. In the past two decades their importance has been properly realized, widely applied and more frequently stressed in the medical literature. Credit for this goes to a number of authors, among them Lippman, Rifkin, Leiter, Volk and Popper, Quinn and Zimmerman, Walz and James and others.[3,5,6,7,8,9] Quinn and Zimmerman[8] in 1954 suggested a classification of droplet-containing epithelial cells into three types.

"Glitter calls," i.e. polymorphonuclear white cells with granules showing Brownian movement, were demonstrated in urinary sediment as early as 1909 by Schilling.[10] It was not until 1949 that the glitter cell, or granular motility cell, was reintroduced to clinical medicine by Sternheimer and Malbin.[11] The same authors described a supravital stain for easier identification of such cells and two years later correlated these cells with the clinical recogniton of pyelonephritis.[12]

The "telescoped urine" seen in the visceral angiitis group of diseases was first described by Krupp[13] in 1943 and repeatedly since confirmed in numerous other reports.

It would be beyond the scope of this paper to discuss the pathogenesis and morphology of all the constituents of the urinary sediment. For this purpose we recommend the outstanding book of Lippman,[3] as well as numerous works of Addis,[14,4] Schreiner[15,16] and others. Our purpose is to emphasize and explain the constituents of urinary sediment which were described relatively recently, and which may not be well understood.

CASTS. The great majority of casts can be recognized by ordinary microscopic technique, preferably under somewhat subdued light. However, various methods were suggested for better identification, i.e. phase-contrast microscopy, polarized-light microscopy, staining with iodine, negative-silhouette staining with India ink, various contrast stains, etc.

The quality of the casts reflect its etiology; the width of the cast is significant prognostically. A **hyaline cast** is the result of precipitation of protein in the tubular lumen. White and red blood cells, as well as epithelial cells, fat droplets and oval fat bodies can be trapped in the hyaline matrix. As the mechanism of proteinuria is not well understood and it appears in various extrarenal conditions, a hyaline cast by itself does not help diagnostically. On the other hand, an **epithelial cast** is of greater importance, as it is formed by conglutination of desquamated epithelial cells. Since tubular epithelium normally desquam-

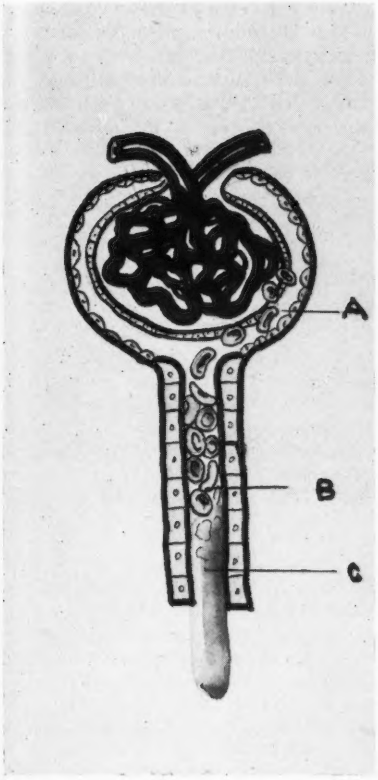

Fig. 1—Stages in the Formation of a Blood Cast.

A.—Discharge of the red blood cells into the tubular lumen through damaged glomerular membrane as in glomerulitis.

B.—Conglutination of the red blood cells in a proteinaceous matrix.

C.—Destruction of erythrocytic cell walls with the formation of a homogeneous orange blood cast.

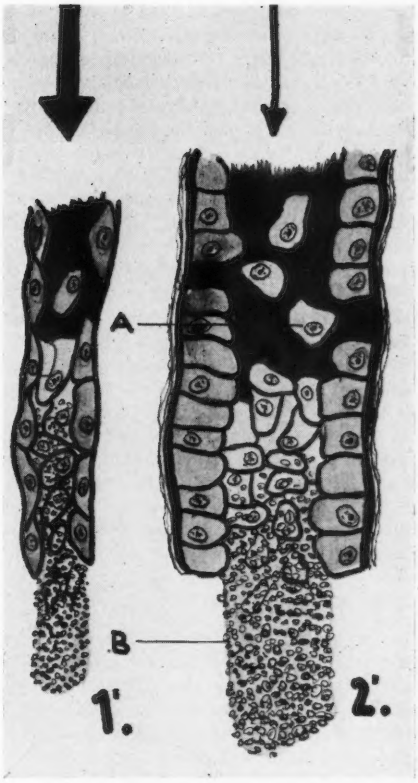

Fig. 2—Comparison of Narrow and Broad Casts (the width of the cast is related to the degree of urinary stasis).

1'—rapid urinary stream in a narrow tubular lumen with fast formation of casts.

2'—slow urinary stream in a wide tubular lumen necessitating marked tubular damage for formation of the cast.

This figure also demonstrates the stages in cast formation from 2'A which show the epithelial cell being incorporated into the cast of 2'B which illustrates the coarsely granular particles being changed into finely granular particles.

ates, an occasional epithelial or granular cast might be expected. However, with increasing tubular damage, these casts become abundant. When the damage is recent, single epithelial cells, their outlines and even nuclei can be clearly recognized within the cast. Occasionally the cellular cast may be seen to consist of two rows of epthelial cells. This is sometimes helpful in differentiating it from a pus cast, where the arrangement of the cells is haphazard. Disintegration of the cells gives successively the picture of a coarsely granular, finely granular and lastly a waxy cast indicating degrees of urinary stasis. A **red blood cell cast,** consisting of intact red cells, must be differentiated from a **blood cast** in which there are no cell margins whatsoever and the color is diffusely orange or red (fig. 1). Though there exists some controversy, the latter is considered more significant of glomerulitis. A possible explanation might be extravasation and

subsequent degeneration of erythrocytes due to impaired tubular urinary flow in severe glomerular disease. **Broad casts** (fig. 2) are invariably associated with some degree of renal failure (though not necessarily with uremia), and therefore they are also termed "renal failure casts." Their width, several times that of ordinary casts, makes their identification simple. Such casts may be again cellular, granular, waxy or mixed with lipoid elements. They are formed in the larger collecting tubules and in the ducts of Bellini where the urinary stream is slow; therefore, considerable destruction of the tubular epithelium is necessary for these cells to be washed out in the urine. The swift urinary stream in narrower tubules, on the other hand, will easily detach even minimally damaged tubular epithelium. There is no close correlation between the percentage of broad casts and the degree of renal failure; however, an increase in the number of such casts is roughly paralleled by an increase in blood urea nitrogen.[4]

It is understandable that as a blood cast is indicative of glomerular damage and an epithelial or granular cast indicative of tubular degenerative changes, a white blood cell cast represents inflammation of the renal parenchyma. Peroxidase staining was recently recommended for the easier identification of the latter.

FATTY ELEMENTS—In addition to varieties of granular casts, fatty elements (oval fat bodies, fatty casts and fat droplets) are presumed to be reflections of renal tubular degeneration.

An **oval fat body** (fig. 3) is regarded as a desquamated tubular epithelial cell which has undergone fatty degeneration before sloughing off into the tubular lumen. Quinn and Zimmerman[8] divided droplets containing epithelial cells into 3 types. A round epithelial cell with only a few droplets was called a type I cell, and a typical oval fat body loaded with droplets was called a type III cell. Type II cell were intermediate in the number of droplets.

Under low power, an oval fat body appears as a dark, almost black body easily misinterpreted as an artefact. It is only when viewed under high power that the glistening, refractile nature of the individual globules becomes apparent. It is not difficult to recognize an oval fat body by ordinary microscopic technique; however, for further identification one may resort either to the use of polarized light, or specific fat stains.

The commonly used stains which stain the majority of fat globules bright red to orange red are Sudan III and Oil Red. The chemical nature of this fat is uncertain, possibly cholesterol esters.[15] After centrifuging the urine, the supernatant is discarded and three drops of Sudan III or Oil Red are added to the sediment. The dye is then mixed with the sediment by briskly flicking the centrifuge tube with the finger several times. For optimal staining, it is best to wait at least ten minutes before examining the drops.

Fatty casts are formed by a conglomeration of oval fat bodies moulded by the tubular lumen. One may also see hyaline fatty casts which are predominantly hyaline casts containing either the intact oval fat body or free fat droplets.

The diagnostic significance of oval fat bodies and other fatty elements is not quite conclusive; however, they are seen abundantly in nephrotic syndromes. In addition, oval fat bodies were described as a constituent of "telescope urines" seen in visceral angiitis[8-13] and severe penicillin hypersensitivity reactions.[8] Type I and type II cells have been described in numerous other conditions such as polycystic disease, pyelonephritis, renal calculi, leukemia, arteriosclerotic heart disease with or without heart failure, hypertensive heart disease, syphilitic aortic insufficiency, febrile diseases, certain metabolic diseases such as diabetes mellitus without Kimmelstiel-Wilson syndrome, Cushing's disease, xanthomatosis and other non-renal diseases.

GLITTER CELLS. Recently attention has turned to a characteristic urinary sediment observed in pyelonephritis. In a classical paper by Sternheimer and Malbin,[11] a characteristic white blood cell was described with peculiar morpho-

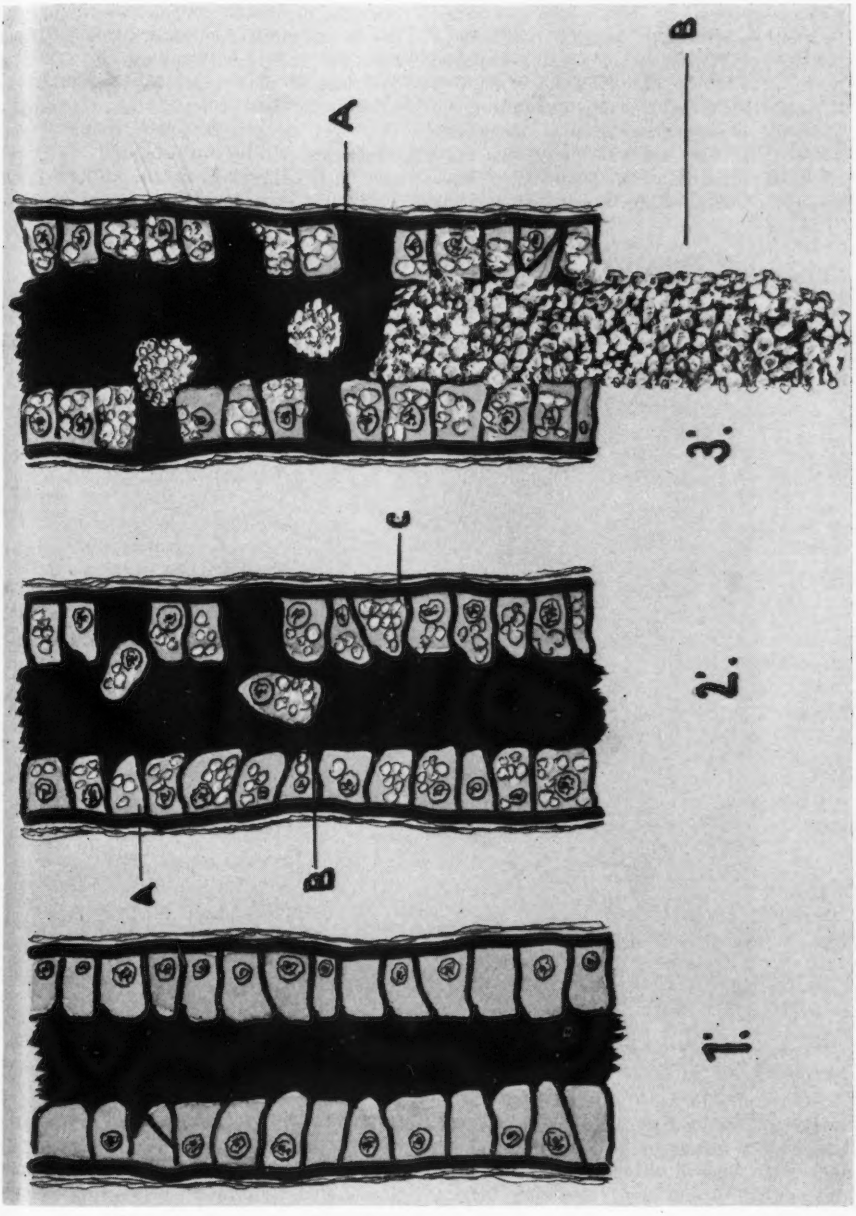

Fig. 3—Oval Fat Bodies and Fatty Casts.

1'—intact tubule.
2'—fatty infiltration of the tubular epithelium.
3' A—Fat laden tubular epithelial cell becoming an oval fat body.
3' B—Conglutination of oval fat bodies becoming a fatty cast.

logical properties. This cell has been termed a "granular motility cell" or a "glitter cell" (fig. 4). When compared with other white cells, this cell is swollen in appearance and the cystoplasmic granules are observed to exhibit Brownian movement. The authors noted its presence in inflammatory renal diseases—abscess of the kidney, acute and particularly in advanced pyelonephritis. Glittering may be seen in an unstained specimen with careful observation under high dry, or oil immersion. However, Sternheimer and Malbin described a special stain composed essentially of saphranin in gentian violet. Using this stain we can differentiate the two major types of white cells: 1) a dark staining cell, the nucleus of which is reddish-purple and the cytoplasm colorless to pink; 2) a pale staining cell, the nucleus of which is colorless to pale blue and the cytoplasm colorless to faint blue with fine granules. The first is seen in lower urinary tract infections, while the second is seen primarily in diseases of the kidney itself. Glittering is seen only in pale staining cells. The staining itself is a simple procedure and is accomplished by merely adding one drop of Sternheimer's solution to the sediment remaining in the bottom of the centrifuge tube after discarding the supernatant. Since the glittering may be seen even in the unstained specimen, one may ask, what is the advantage of staining. New light has been

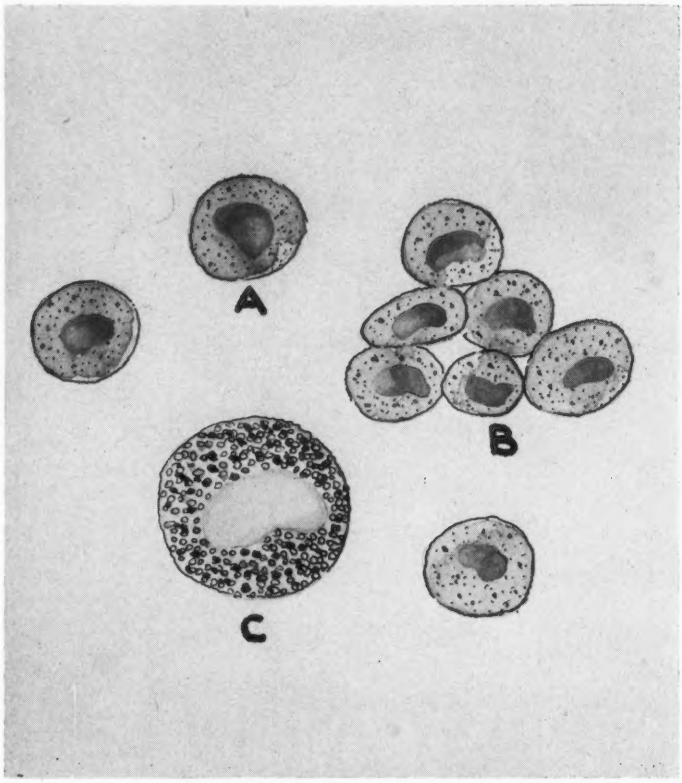

Fig. 4—Comparative size and staining qualities of polymorphs (A and B) of non-renal origin with a glitter cell (C) of renal origin (size slightly exaggerated).

shed on this subject by the more recent investigations by Porrier and Jackson.[17] They stressed the importance of the staining properties as compared to the presence of granular motility. Granular motility is seen only in urines having a specific gravity of 1.019 or less, i.e. dilute urines. Since in early stages of pyelonephritis, the specific gravity of the urine is not yet impaired, glittering may not be present. A more constant feature of these pus cells is therefore the manner in which they take up the stain, which is independent of specific gravity.

It is conceivable that younger white cells representing acute or active inflammation have cell membranes relatively impermeable to the stain, hence the pale staining qualities.[17] Great variation may be seen in the degree of granular motility; in some cells motility may be limited to a focal area of the cytoplasm. Repeated examinations of the urine in suspect cases of pyelonephritis are sometimes necessary to establishing the diagnosis microscopically, since only 66% accuracy can be expected with a single examination.[17] The glittering has been seen in urines kept in the refrigerator up to one week.[12]

We have found the Sternheimer stain technique to be simple and invaluable in recognizing previously unsuspected cases of pyelonephritis.

URINARY SEDIMENT AND CLINICAL CORRELATION. Before properly interpreting urine sediment, one must understand the pathogenesis of various renal diseases. Proteinuria and many white cells, some of them in clumps in a patient exhibiting other symptoms of an acute pyelonephritis, will only confirm the anticipated diagnosis. However, awareness of "glitter cells" and possibly the use of Sternheimer's stain might solve the diagnostic riddle of a case with azotemia of unknown origin with only an insignificant number of white cells in the sediment. Broad casts in the same patient at a later date will indicate progression of the disease. Many red blood cells, epithelial and hyaline casts and blood casts will provide a clue to the diagnosis of acute glomerular nephritis. Other conditions which might give a similar urinary sediment picture must be ruled out by using the clinical information: embolic glomerulitis as seen in subacute bacterial endocarditis or in septicemia; parasitic diseases as Schistosomiasis; neoplastic renal diseases; drug hypersensitivity; malignant hypertension or renal calculi. Massive proteinuria with numerous fatty elements will certainly help in diagnosing a nephrotic syndrome, but it will not specifically point to the type of disease such as lipoid nephrosis, intercapillary glomerulosclerosis, renal amyloidosis, chronic glomerular nephritis, toxemia of pregnancy or renal vein thrombosis. A "telescope urine" consisting of blood casts, fatty elements and broad casts, all of these present in approximately equal proportions, will help confirm the diagnosis of a suspected case of systemic lupus erythematosus or periarteritis nodosa. Positive Prussian Blue reaction of yellow brown coarse pigment granules might clinch the diagnosis of hemochromatosis.

In renal neoplasms, polycystic disease, developmental anomalies, nephrosclerosis, renal vascular involvement, chronic passive congestion and numerous other renal and extrarenal diseases, there are no characteristic sediments whatsoever; nevertheless, the microscopic examination might help us to understand the disease, its natural course and complications.

Relatively little is known about the cytoplasmic inclusion bodies described in various virus infections; however, recent reports are encouraging[18] Perhaps the same can be said about the cytological examinations of fixed-stained smears of urinary sediments for malignant cells.

We neither wish to exaggerate the diagnostic importance of examination of the urine, nor stimulate any over-interpretation. The sole aim of this paper is to try to raise the "lost art of urinalysis" to where it belongs. It is a very valuable and simple laboratory test, frequently helpful and sometimes indispensable. Should this be remembered, the purpose of this paper is achieved.

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ADYNAMIC ILEUS *

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Intestinal obstruction may be defined as a failure of the normal progression of the fecal stream toward anal elimination. This may be generally classified into three main types:

1. **Mechanical obstruction** where there is occlusion of the lumen of the intestine which may be acute or chronic.

2. **Vascular obstruction** (intestinal strangulation) in which there is occlusion of the mesenteric blood supply;

3. **Adynamic ileus** (often referred to as paralytic, inhibition, neurogenic or physiologic ileus) in which peristaltic propulsion has failed, causing the intestinal contents to be stagnant as if the lumen were occluded, but with no organic obstruction. Thus, by definition, adynamic ileus may be considered to be a form of intestinal obstruction.[1-4]

The basic etiology of motility disturbance in adynamic ileus is unknown. The inherent myogenic contractility of the intestine remains unimpaired. Perhaps there is a parasympathetic-sympathetic nerve imbalance.[5] The muscles and the parasympathetic nerves which stimulate intestinal motility are not paralyzed; however, it may be that there is a reflex hyperactivity of the sympathetic nerves. The experimental evidence seems to confirm this concept, but clinical proof has been lacking in that spinal anesthesia and sympathetic blocks are no longer used in the treatment of this condition.[6] Perhaps the ionic balance of such elements as potassium and sodium play a role in the pathogenesis.

Patients with deficiencies of potassium and sodium often respond rapidly to adequate parenteral replacement therapy. However, it is difficult to explain the rapid distention in some instances such as acute pancreatitis where adequate time has not passed for an electrolyte imbalance to develop. There may be more than one factor involved in the pathogenesis.

Adynamic ileus may be caused by extra-abdominal as well as intra-abdominal conditions. Faulty pre- and postoperative management may be predisposing factors. Among the extra-abdominal factors (Table I.) are those of the toxic group which includes uremia, systemic infections, pneumonia, empyema, meningitis and septic conditions. Electrolyte imbalance may be associated with adynamic ileus, particularly in a patient who has been on constant gastric suction without potassium replacement. Hypokalemia, hyponatremia, oligemia, hypoproteinemia and avitaminosis may cause adynamic ileus. In the metabolic group of etiological factors are porphyria and myxedema. The neurogenic entities include lead poisoning, spinal cord lesions, damage to the central nervous system, skeletal trauma involving nerve roots, fracture of ribs, thoracoplasty, fracture of spine, hyperextension in a plaster cast. Muscular trauma, particularly of the back muscles, may also be a factor. Certain drugs used in the treatment of hypertension, e.g. Ansolysin® and hexamethonium as well as prolonged ether anesthesia, particularly when the gastrointestinal tract is inflated by bag pressure, may produce adynamic ileus.[7] There are some of the less common conditions in which adynamic ileus may be secondary to the disease, such as disseminated lupus erythematosus, affecting primarily the duodenum and jejunum.[8] Pseudomembranous enterocolitis as well as allergy may also be associated with this condition.[9]

The intra-abdominal causes of adynamic ileus are summarized in Table II. These fall into three main groups—peritoneal irritation, extraperitoneal irritation and vascular changes. Peritoneal irritation may be traumatic due to operation (rough handling of viscera) or to blunt trauma (non-operative) particularly after automobile accidents. Ady-

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Table I.

EXTRA-ABDOMINAL CAUSES OF ADYNAMIC ILEUS.

I. Toxic
- A. Uremia
- B. Systemic infections
- C. Pneumonia
- D. Empyema
- E. Meningitis
- F. Septic Conditions

II. Nutritional
- A. Electrolyte Imbalance—K, Na, Cl
- B. Oligemia-hypoproteinemia
- C. Avitaminosis

III. Metabolic
- A. Porphyria
- B. Myxedema

IV. Neurogenic
- A. Lead poisoning
- B. Spinal cord lesions
- C. Damage to central nervous system
- D. Skeletal trauma involving nerve roots
  1. Fracture of ribs
  2. Thoracoplasty
  3. Fracture of spine

V. Muscular trauma of back

VI. Drugs
- A. Those used for hypertension such as Ansolysin® and hexamethonium
- B. Prolonged ether anesthesia

VII. Allergy

namic ileus usually follows abdominal surgery for periods of 24-72 hours. Chemical peritonitis leading to ileus may follow the escape of irritating fluids such as gastric contents, bile, pancreatic fluid, urine or blood into the peritoneal cavity. Gall bladder colic and pancreatis as well as bacterial peritonitis may be associated with adynamic ileus. Extraperitoneal irritation may be caused by hemorrhage, infection, renal and ureteral lesions, renal colic and retroperitoneal trauma. Vascular changes may also be a cause of adynamic ileus. Mesenteric thrombosis, both arterial and venous, as well as embolism may be associated with this condition. Thrombosis of the superior mesenteric vein, usually secondary to non-penetrating abdominal trauma, may occur during a period varying from shortly after injury to several weeks later. Strangulation which produces vascular changes (omental strangulation, torsion of an ovarian cyst or stangulation of the spermatic cord) as well as prolonged simple obstruction and arteriosclerotic abdominal aneurysms may lead to adynamic ileus.

Table II

INTRA-ABDOMINAL CAUSES OF ADYNAMIC ILEUS

I. Peritoneal irritation
- A. Traumatic
  1. Non-operative
  2. Operative
- B. Chemical peritonitis
- C. Bacterial peritonitis

II. Extraperitoneal irritation
- A. Hemorrhage
- B. Infection
- C. Renal and ureteral lesions
- D. Retroperitoneal trauma

III. Vascular changes
- A. Mesenteric thrombosis (arterial and venous)
- B. Embolism
- C. Strangulation
- D. Prolonged simple obstruction
- E. Arteriosclerotic abdominal aneurysms

Pathologically the entire intestinal tract may be distended, but the distention usually begins in the ileum and may extend throughout the small bowel. This is due to the accumulation of fluid and gas from swallowed air, putrefaction and interference with gaseous absorption. Pressure within the intestine is much less in adynamic ileus than in mechanical obstruction, and rupture of the bowel seldom occurs. The colon may be of normal size. The bowel wall may be stretched sufficiently to cause the same sequence of events as occurs in mechanical obstruction—stasis, distention, fluid and electrolyte loss, chemical changes in the blood, etc.

The diagnosis of adynamic ileus occasionally presents a difficult program to

the surgeon when he is faced with the triad of obstipation, distention and vomiting. Adynamic ileus may simulate, mask or precipitate small bowel obstruction. Sometimes, when the ileus is being relieved pain may be present, simulating mechanical obstruction. In addition, the x-ray pattern may be similar. If obstruction is associated with strangulation, secondary adynamic ileus may develop to mask the x-ray pattern of obstruction by producing a non-specific distention pattern. Adynamic ileus may also initiate small bowel obstruction where there is a kink or adhesion which only produces partial luminal occlusion (partial obstruction progressing to complete). If the ileus causes a volvulus of the cecum, sigmoid or splenic flexure a large bowel obstruction will ensue. Often a prolonged paralytic ileus is associated with evisceration.[10] The distention in adynamic ileus may be great enough to interfere with respiration and may impede venous return from the lower extremities.[11]

The differential diagnosis between adynamic ileus and mechanical obstruction can usually be made without too much difficulty. The clinical impression should be predominant. A good history is important. Possible eitologic factors may be elicited. The onset is usually within the first three postoperative days whereas mechanical obstruction occurs between the sixth and tenth postoperative days. Pain is usually absent, whereas in mechanical obstruction it is of the colicky or cramping type. Bowel sounds are frequently absent, which is one of the most important points in the differential diagnosis,[12] as they are hyperactive initially in mechanical obstruction. Occasionally in adynamic ileus the bowel sounds are feeble and high pitched which may add to the difficulty in diagnosis. Vomiting is present and is of the regurgitant or overflow type as contrasted to being forceful in mechanical obstruction. Rectal examination reveals the ampulla to be dilated in adynamic ileus, whereas with mechanical obstruction the rectum usually collapses against the examining finger. If there is no peritonitis or infection, the white blood count will not be elevated. In mechanical obstruction the white blood count may be normal or mildly elevated (10-12,000), whereas in the presence of strangulation obstruction or thrombosis it is elevated to a higher degree earlier in the disease (15-30,000).

X-ray examination may not be of much help on occasion; however, sometimes it is decisive. Careful taking of x-rays in different positions with thoughtful analysis and repeat examination when necessary may aid one to arrive at a proper diagnosis in several instances. There is moderate generalized dilatation of the gastrointestinal tract (gas in large and small intestine) in adynamic ileus, whereas in mechanical obstruction the dilatation is usually proximal to the obstruction. Fluid levels may be present in both adynamic ileus and mechanical obstruction; however, a specific type of fluid level (the "dynamic loop") is seen in mechanical obstruction, but not in adynamic ileus.[13] A barium enema may be utilized in the differentiation of the two conditions. The proper diagnosis is often made on the clinical impression, but in difficult cases the radiologist may be of definite aid.

If the patient has a tube in the gastrointestinal tract the amount of aspirate will be less than the fluid he takes by mouth (positive balance) in a case of adynamic ileus. However, with mechanical obstruction more fluid is recovered than is taken by mouth (negative balance). This gastric balance is usually measured for a period of 24 hours.[14] If the intestinal tube is clamped for a few hours the patient with mechanical obstruction may experience colicky pain. Table III summarizes the points in the differential diagnosis.

To properly manage adynamic ileus, remove or treat the underlying cause. Prevent this condition from occurring if possible. This means adequate pre- and postoperative care with particular attention to restoring the paitent's nutritional status (fluid and electrolytes, blood volume, vitamins). Proper surgical technique should be observed paying particular attention to asepsis, hemostasis and gentle handling of tissues. During the first 8 to 12 hours postoperatively, excess fluid by mouth should be avoided as this may lead to air swallowing. In

Table III.

DIFFERENTIAL DIAGNOSIS OF ADYNAMIC ILEUS AND MECHANICAL OBSTRUCTION

	Adynamic Ileus	Mechanical Obstruction
Onset	Usually within 1st three postoperative days	Usually from sixth to tenth postoperative day
Cramping pain	Absent	Present
Distention	Present	Present
Obstipation	Present	May have had bowel movement prior to onset
Vomiting	Regurgitant or overflow type	Forceful
Bowel sounds	Absent	Hyperactive initially
Gas pattern	Generalized dilatation	Dilatation proximal to obstruction
Rectal examination	Ampulla dilated	Rectum usually collapses against examining finger
Leucocyte count	Not elevated if no peritonitis or infection	May be normal or mildly elevated (10-12,000). Higher in presence of strangulation obstruction or thrombosis early (15-30,000).
Amount of gastrointestinal aspirate	Less	Greater

instances where postoperative adynamic ileus is anticipated, an intestinal tube with continuous suction should be utilized preoperatively, at operation and postoperatively until bowel sounds have returned and the patient has passed gas. It is desirable to avoid preoperative purgation with cathartics. Morphine tends to perpetuate an ileus,[15] retarding the propulsion of the material along the intestinal tract. Likewise, the repeated use of peristaltic stimulant drugs is undesirable.[16]

The management of an established adynamic ileus is often not difficult. Intubation of the stomach and intestine with suction is a sound principle. A rectal tube may also be of value. Oral intake is limited. Fluid and electrolyte balance is strictly maintained on an

intake-output basis, particular attention being given to sodium, potassium, chlorides, proteins, and circulating blood volume. In the face of poor renal function potassium must be administered with great care. Five to seven days of conservative management should be the maximum period required for complete decompression of adynamic ileus. Operative intervention (rarely necessary) should be undertaken to relieve the distention after the maximum period has elapsed.

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THERAPEUTIC ABORTION

A 5-Year Survey at Mount Sinai Hospital

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The subject of therapeutic abortion (TA) has always been controversial. In any group discussion there is invariably wide divergence of views.[2,4,5] Almost always the physician who suggests a TA is put on the defensive by his colleagues and is often regarded as an ogre by certain segments of the public—so much so that legislation has been passed by most states regulating TA.

TA is the artificial termination of pregnancy for medical reasons. There are many qualifications of this definition. Some of the more important limitations are:

Therapeutic implies that unless the pregnancy is terminated the patient will become dangerously ill or that a disease already present will become materially worse. The one exception to this definition is related to German measles (rubella). In this condition abortion destroys the fetus which has been irreparably damaged by the rubella virus acquired by the mother.

Abortion is the termination of pregnancy prior to the 20th week of gestation. TA can only be performed by a licensed physician in a registered hospital. Prior to 12 weeks' gestation the usual procedure is the operation called dilatation and curettage (D & C). Pregnancies of longer duration than 12 weeks are terminated by (1) vaginal hysterotomy or (2) abdominal hysterotomy. If it is deemed necessary to eliminate the possibility of future pregnancies sterilization can be accomplished at the time of TA. Sterilization can be performed by: (1) tubal ligation via posterior colpotomy at the time of D & C; (2) tubal ligation at the time of vaginal or abdominal hysterotomy; or (3) vaginal or abdominal hysterectomy.

Artificial termination as used in this paper means the destruction of a pregnancy and/or its removal from the uterus. Radium or x-ray has been occasionally used for this purpose incidental to treatment of cancer of the uterus. With this one exception, the surgical methods described previously are the only procedures employed at present. There are no other means of safely terminating a pregnancy.

Medical reasons include the indication for the abortion. Many state laws make the general statement that TA may only be performed if it is life-saving; others state that the abortion must prevent mental or physical illness.

Since TA can only be done in hospitals, the responsibility for policing has fallen on the shoulders of hospital administrators and their advisors[3].

At Mount Sinai Hospital until 1957 the rule prevailed that a TA could be done if two consultants concurred in written consultations. On January 1st, 1957 the regulation was changed to: The patient must be admitted to the hospital. The results of the history and physical examination then is submitted to an anonymous committee composed of three consultants selected by the director of the hospital. If the opinions of the consultants are unanimous in favor of abortion the director then grants permission.

The hospital records of patients who had had TA in the years 1955-59 were pulled from file and certain information was tabulated. (Table 1) Figure 1 graphically illustrates the incidence of TA during these 5 years; the number of TA was lowest in 1957. This might or might not have been related to the establish-

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TABLE I

THERAPEUTIC ABORTIONS

1955

NO.	AGE	GRAV.	PARA	RACE	STATUS	PRINCIPAL INDICATION FOR ABORTION	DURATION OF GESTATION	METHOD OF ABORTION	STERILIZED?
1	39	III	II	W	M	both children idiots	14 weeks	abd. hysterectomy	yes
2	22	II	I	W	M	rheumatic heart disease	8 weeks	D & C	no
3	36	II	I	W	M	coronary heart disease	8 weeks	abd. hysterectomy	yes
4	26	V	IV	W	M	3 children deaf-mutes	8-10 weeks	D & C	yes
5	25	IV	III	W	M	3 children mongoloids	18-20 weeks	abd. hysterectomy	yes
6	30	I	O	W	M	Chr. Glomer. nephritis	8 weeks	D & C	no
7	34	III	II	W	M	Fusion & Gibbus, Spine	10 weeks	abd. hysterectomy	yes
8	36	II	I	W	M	Nephrectomy, Tb. Kidney	6 weeks	D & C	yes
1956									
9	33	IV	III	W	M	German measles	8-10 weeks	D & C	no
10	42	IV	III	W	M	Spinal fusion	6 weeks	D & C	yes
11	33	I	O	W	S	Depression reaction – Suicidal attempt	8-10 weeks	D & C	no
12	32	II	I	W	M	Brain tumor; hemiparesis	16 weeks	Abd. hysterectomy	yes
13	35	IV	III	W	M	Depressive psychosis; suicidal tendency	10-12 weeks	D & C	no
14	26	III	II	W	M	Ca of breast	10 weeks	Abd. hyster. and oophorectomy	yes
15	28	IV	III	W	M	German measles	12 weeks	Vaginal hyster.	no
16	32	III	II	W	M	Tb. of ankle	8-10 weeks	D & C	no
17	30	II	I	W	M	Myasthenia gravis	6-8 weeks	D & C	no

NO.	AGE	GRAV.	PARA	RACE	STATUS	PRINCIPAL INDICATION FOR ABORTION	DURATION OF GESTATION	METHOD OF ABORTION	STERILIZED?
1956									
18	25	III	II	W	M	Schizophrenia	14-16 weeks	Abd. hysterotomy	yes
19	23	II	I	W	M	Bilat. hydronephrosis	10-12 weeks	Abd. hysterotomy	yes
20	24	III	II	W	M	Schizophrenia	16 weeks	Abd. hysterotomy	yes
21	31	IV	III	W	M	Rheum. heart disease	12 weeks	Abd. hysterectomy	yes
22	38	V	III	W	D	Rheum. heart disease	14 weeks	Abd. hysterectomy	yes
23	29	V	IV	W	M	Schizophrenia	12 weeks	Abd. hysterotomy	yes
1957									
24	31	III	O	W	S	Malignant hypertension	6 weeks	D & C	yes
25	37	III	II	W	M	German measles	10-12 weeks	D & C	no
26	17	I	O	W	S	Pregnancy by incest	12 weeks	D & C	no
1958									
27	33	II	I	W	M	German measles	6-8 weeks	D & C	no
28	35	IV	II	W	M	Femoral thrombosis	9 weeks	D & C	no
29	36	III	II	W	M	Pulmonary embolism Rheum. heart disease	9 weeks	D & C	yes
30	25	II	I	W	M	German measles	13 weeks	D & C	no
31	32	V	III	W	M	German measles	7 weeks	D & C	no
32	27	V	II	W	M	German measles	10 weeks	D & C	no
33	38	V	IV	W	M	Last 3 babies died of erythroblastosis	10 weeks	D & C	yes
34	33	IV	II	W	M	Nephrosis	6-8 weeks	D & C	yes
35	35	I	O	W	D	Excessive diagnostic x-rays	6-8 weeks	D & C	no

NO.	AGE	GRAV.	PARA	RACE	STATUS	PRINCIPAL INDICATION FOR ABORTION	DURATION OF GESTATION	METHOD OF ABORTION	STERILIZED?
1958									
36	22	I	0	W	M	German measles	6 weeks	D & C	no
37	29	V	III	W	M	German measles	10 weeks	D & C	no
38	35	II	I	C	M	Tbc; pneumonectomy	14 weeks	Abd. hysterotomy	yes
1959									
39	37	IV	II	W	M	Severe mental depression	6 weeks	D & C	yes
40	30	IV	III	W	M	Hypertensive vasculo-renal disease	10 weeks	vaginal hysterectomy	yes
41	37	III	II	W	M	Severe mental depression	7 weeks	D & C	yes
42	33	IV	III	W	M	Suicidal depression	8 weeks	D & C	no
43	34	IV	III	W	M	German measles	8 weeks	D & C	no
44	39	V	IV	W	M	Pregnancy following rape	12 weeks	D & C	no
45	24	I	0	W	M	Toxoplasmosis	10 weeks	D & C	no
46	37	IV	II	W	M	Ca breast; rad. mastec-tomy 1 year ago	10 weeks	Abd. hysterectomy and oophorectomy	yes
47	45	V	IV	W	M	Depressive psychosis	8-10 weeks	Vaginal hysterectomy	yes
48	18	I	0	W	S	Psychopathic personality; miscegenation	6 weeks	D & C	no
49	34	IV	III	W	M	Severe mental depression	17 weeks	Abd. hysterectomy	yes
50	32	IX	VIII	C	M	Malignant hypertension	10 weeks	D & C	yes
51	28	III	II	W	M	Psychoneurosis; depression	15 weeks	D & C	no

W=white; C=colored; S=single; M=married; D & C = dilatation and currettage; D=divorced

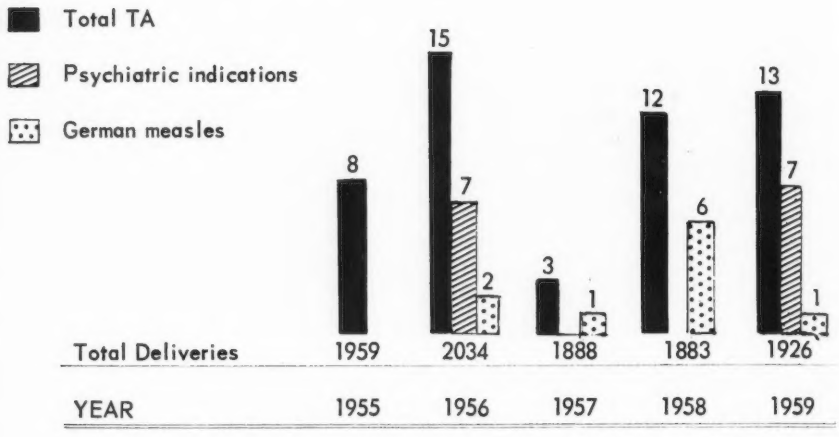

Fig. 1. Indications for Therapeutic Abortions, 1955-59.

ment of stricter regulations. Subsequently the incidence rose to prior levels.

In this five-year period there were 9,580 deliveries and 51 TA's; the rate of TA was about 5 per 1000 deliveries. In comparison to statistics in the literature our incidence was very low. However, it must be emphasized that the frequency of TA generally is less every year; there seems to be less indication. The ratio of TA performed to the number of rejected applications would be of interest; unfortunately the number of requests denied was unavailable. The fate of the patients rejected is unknown; a follow-up of these patients might reveal some answers to many questions, e.g. were those patients aborted elsewhere; what was the course of the disease in those women who were not aborted; how many of our aborted women had subsequent pregnancy?

Table 1 includes only the barest information of each TA. To discuss each problem in its entirety is beyond the scope of this paper. It must be emphasized that each patient was considered as an individual in a life situation and not merely as a clinical entity. The principal indication was always related to other factors such as the obstetric history, the marital, social, economic status and other associations. There is no situation in the practice of medicine where the knowledge of all aspects of the case is so important as in TA. Here is where the family doctor plays the most important role.

COMMENT

Of the 51 TA in this survey 14 (29.8%) were performed because of mental or nervous disease; 10 (20%) of the abortions were performed because the mother had acquired German measles in the first trimester. (Table 2.) Sterilization was performed in 27 patients (53%).

In case No. 35 the patient had received a complete G.I. series of x-rays, gallbladder x-rays and x-rays of the G.U. tract; then it was discovered that the patient was pregnant.

The opinions of TA vary in a broad spectrum from the viewpoint which is opposed to the willful, premeditated destruction of a living human embryo or fetus—to the other extreme view which approves or advocates legalized abortions. Therapeutic abortion as discussed in this paper seems to be a rational middle ground.

It is sometimes necessary to remind the medical profession and the public that doctors are law-abiding citizens. In good conscience doctors sometimes recommend TA. Admittedly our judgment

is not infallible nor is our knowledge omniscient. Safe-guards in the form of mandatory consultations and anonymous committees have been established; these safe-guards should be considered not as obstacles but as screening measures assuring compliance with the law and furthering the confidence of the public.[6,7]

Hospitals and their representatives enjoy the confidence of the practicing physician. Both are aware that there is a job to be done: to preserve and promote health.

SUMMARY

In a 5-year period (1955-59) at Mount Sinai Hospital 51 therapeutic abortions were performed; there were 9580 deliveries during this time. Psychiatric conditions was the most common indication for TA; German measles was second in frequency. The modus operandi of TA at Mount Sinai Hospital is described.

TABLE 2.

Incidence of Principal Indications for Therapeutic Abortions

INDICATION	No. of Cases
Nervous & Mental	14
German Measles	10
Hypertensive cardio-vascular	5
Rheumatic heart disease	4
Kidney disease	4
Mental disease in children	4
Tuberculosis	2
Carcinoma of breast	2
Spinal disease	2
Toxoplasmosis	1
Rape	1
Incest	1
Excessive diagnostic x-rays	1
TOTAL	51

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CARCINOID TUMORS OF THE GASTROINTESTINAL TRACT

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Carcinoid tumors are no longer to be regarded as quaint neoplasms which are only occasionally malignant or which have a quiet, protracted course. The incidence of malignancy has been reported to be as high as 60%,[1] and this is probably directly proportional to the time of onset and the start of treatment. Thus, carcinoid of the appendix, which produces appendiceal obstruction and appendicitis early, is probably removed before malignant changes or invasion have occurred. When carcinoid occurs in a more "silent" portion of the gastrointestinal tract, i.e. the duodenum or ileum, the chances of the tumor being malignant are much greater.

Carcinoid may be found in any age group, from ten days to eighty nine years,[2] although appendiceal carcinoid is most commonly seen in patients under thirty; for those with carcinoid outside the appendix the average age is fifty-five to sixty.[3] The occurrence of multiple carcinoid is certainly not uncommon having been reported to be as high as 33%.[4,5]

Early, the tumor is a small, firm, well-circumscribed mass which has a distinct, easily recognizable yellow color; later these may extend from their submucosal position to involve all layers of the bowel wall. Direct extension to adjacent mesentery produces a prolific fibrous tissue reaction several times the size of the tumor, and this is a frequent cause of small bowel obstruction when carcinoid is present in the ileum.[6] In appendiceal carcinoid the tumor is situated at or near the tip in about 90%[2] of cases and, at the operating table, is often mistaken for a fecolith. Extra-appendiceal carcinoids of the gastrointestinal tract project into the lumen of the bowel as single or multiple sessile nodules.

Histologically, the carcinoid tumor is composed of islets of epithelial cells which are small, polygonal or round, surrounded by a fibrous stroma and containing a few to several mitotic figures. The nuclei are round or oval and basophilic, and are surrounded by acidophilic cytoplasm containing granules which take an argentaffin positive stain when treated with ammoniacal silver nitrate. Some carcinoids, notably those in the rectum, do not possess the argentaffin staining quality.[7]

Carcinoid tumors are seldom diagnosed preoperatively, except in the rectum where they cause rectal bleeding and are seen and biopsied through the proctoscope. However, they occasionally give rise to a group of signs and symptoms which may alert the clinician to their presence. This group of signs and symptoms is alluded to as the "carcinoid syndrome" and is caused by the excessive secretion of serotonin by the tumor and/or its metastases.

During the latter part of the nineteenth century observations were made on a vasoconstrictor substance isolated from clotted blood. In 1948, this substance, 5-hydroxytryptamine, was recovered in its pure form and named serotonin.[8] Serotonin is widely present throughout the body, but it is found chiefly in the argentaffin cells of the gastrointestinal tract and in relatively large amounts in platelets.

The malignant carcinoid syndrome is characterized by flushing, recurrent attacks of cyanosis, wide blood pressure fluctuations, tachycardia, tachypnea, asthmatic attacks, diarrhea, telangiectasias and, frequently, signs of pulmonary stenosis with right heart failure. Autopsy reveals right-sided endocardial fibrosis with valvulitis, resulting in pulmonary stenosis and tricuspid insufficiency. None of these pathological findings have been found in the left heart except in the presence of left-to-right shunts.

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It has been established that the lungs are rich in monamine oxidase, an enzyme capable of detoxifying serotonin to 5-hydroxyindolacetic acid (5-HIAA), an inert product found in the urine of patients with carcinoid syndrome. Serotonin is derived from the amino acid tryptophane and,[9] since tryptophane is essential for the synthesis of niacin, it becomes understandable why pellagra is sometimes seen in patients with carcinoid. Pressure or massage of the tumor, with its resultant liberation of serotonin, may produce palpitation, tachycardia and flushing;[10,11] undue excitement or alcohol ingestion[12] may produce a similar effect. Bananas, rich in serotonin, are capable of causing these symptoms in the carcinoid patient.

Treatment of carcinoid is always surgical excision. When located at or near the tip of the appendix appendectomy with removal of the mesoappendix is adequate; however, when the tumor is in the base of the appendix right hemicolectomy is indicated. Carcinoid of the rectum is best treated with abdomino-perineal resection if the tumor is more than 2 cm. in diameter or if ulceration and/or infiltration has taken place. It should be stressed that carcinoid anywhere in the gastrointestinal tract be treated with adequate resection.

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THE DYNAMICS OF A GROUP PSYCHOTHERAPY PROGRAM WITH NARCOTIC ADDICTS

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In the United States, addiction to heroin is associated with urban living,[1] socially and economically depressed neighborhoods,[2] familial disorganization and psychological marginality.[3] While mental illness is a correlate of addiction,[1,4] addicts are rarely psychotic. Statistically, Chicago ranks second in the nation as a center for drug addiction.[5] In spite of this problem, as of this writing there is no money spent by the State of Illinois for the psychiatric treatment of addicts. Estimates of the number of addicts in Chicago generally exceed 6,000.[5] Till July 1, 1959 two treatment centers for narcotic addicts existed in Chicago, Provident Hospital outpatient clinic and the Medical Counseling Clinic at Cook County Jail. The clinic existing at the Cook County Jail was originally administered by Northwestern Medical School under the direction of Dr. Abrams.** This clinic carried on a research and treatment program. The research phase of the project examined narcotic addiction as an epidemiological problem. The treatment phase of the program provided group psychotherapy for incarcerated addicts. Previous articles by Abrams have dealt with the etiology of addiction, the inpact of incarceration on the addict, and the efficacy of a group psychotherapy programs at Cook County Jail. These articles state that:

1. Narcotic addiction among Negroes is a result of psychosocial marginality[6] (which Durkheim has described as Anomy[7]).

2. While incarceration results in alteration of personality, it also increased probability of readdiction after release from jail.[8]

3. A group psychotherapy program aimed at reducing the marginality of the addict by making him more aware of his environment and helping him to struggle with his problems results in the rehabilitation of about 40% of the participants.[9]

This article describes the group psychotherapy program for narcotic addicts at Cook County Jail carried on by the author from September 1958 until July 1959. It details the content and method used to change the narcotic addict from being ultraindividualistic and anti-social in his orientation to an individual capable of functioning effectively in a group. In addition, the goal of the group meetings was to alter the behavior of the addict from a person who used the narcotics to escape from his problems to a person willing and able to struggle effectively with his problems.

Population Sample

Two groups of 13 male Negro addicts and 2 male white addicts met twice weekly for two hours in a 7′ x 9′ cell with the author. The mean age was 27 with a range of 18 years to 65 years. The men were of normal intelligence with an average of 10 years of schooling. They were all born and/or brought up in Chicago. None were psychotic. All but three had been in jail before. The men volunteered for therapy. All were physiologically withdrawn from narcotics for at lease three months before starting therapy. The groups were not intact for the eleven months, i.e. new members were admitted to the group as old members were released from jail. The mean length of time spent in therapy was 6 months. The men in therapy were not usually housed together. About one-third of the men in therapy had jobs in the jail; the remainder sat in their dormitories when not in therapy. New members for therapy were selected by the therapist from a waiting list of about 30 names. A

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prisoner got his name on a waiting list by submitting his name to the therapist. Selection for therapy was on a "first come first served" basis provided that: 1. the applicant had already been sentenced (the jail housed many men who were waiting to be sentenced); 2. there was no evidence of psychosis; and 3. there would be from two to twelve months before release.

Procedure

Group psychotherapy with narcotic addicts is a technique in which a psychotherapist attempts to alter the personality of an individual with a history of addiction, assisting a group of addicts to provide the motivation for, and an atmosphere conducive to the replacement of unhealthy and inadequate behavior patterns by new, more adequate forms of behavior. Much has been written on the problem of addiction, group psychotherapy in general[10] and group psychotherapy with narcotic addicts in particular.[11-16] Because psychotherapy is an art, it is difficult for the author to convey to the reader exactly or even the essence of what transpires in group psychotherapy with narcotic addicts. This is even more difficult to accomplish when we attempt to describe the significant facets of group psychotherapy. In a group situation, not only do you have to consider the interaction of the therapist and patient (as exists in individual psychotherapy), but in addition the interaction of the patient with the group must be taken into account. The need of the psychotherapist to assume the role of scientist compels him to describe the process of group psychotherapy objectively and if possible, operationally.[17] The methods used to describe small group interaction are based on a theoretical framework which places heavy emphasis on the analysis of how people communicate with one another, how effective a group is in solving its problems (co-operatively) and the problems the group chooses to work on. Behavior may be examined and analyzed in terms of what is done—**the content,** and how it is done—**the process.**[18] For example, during one of the psychodramatic sessions the men acted out a situation in which two male addicts attended a party given by non-addicts.* The presentation contained many conflict situations and was concluded by a non-addict shooting the addicts. An analysis of the content of this psychodramatic session would include what each of the members said and did. This would include the topics of conversation and such expressed attitudes as: "squares (non-addicts) have contempt for us because we are junkies (addicts); it's okay to take advantage of people because the world is a jungle; the only way a junkie can make out (hold his own) with the righteous (non-addict) world is to have class (material possessions)."

An analysis of the process would describe who said what to whom, which members took which sides in the arguments which ensued, how each of the members encouraged or discouraged participation by their supporters or antagonists in the arguments which took place, the nature of the struggle for power in the group, and the problems the group chose to work on. These techniques helped the group psychotherapist apply the rudiments of the scientific method (objective description) to his understanding of group behavior. While research involving larger sampling and objective criteria is necessary to confirm the observations presented in this paper, they are nevertheless reported herein, as it is felt that it is clinical data which highlights certain facets of the problem of narcotic addiction and its treatment.

Observations

If the reader had been able to observe group therapy for narcotic addicts at Cook County Jail, several things would have been obvious. He would have seen 7 to 15 men (not all members attended every session) in a cell listening to music, reading poetry, talking about whatever interested them at the moment, and participating in psychodramatic expressions of their problems. The music varied from Charlie Parker to Huddie Ledbetter; the poetry from Langston Hughes to Robert Burns and Walt Whit-

* Psychodrama is a psychiatric technique in which the participants assume certain roles relevant to a particular situation and then act it out, making up their lines as they go along.

man; the topics of discussion from the rumors of contraband operation within the jail to the relative merits of different coital positions and the "fears of going crazy".

Participation in group therapy over a long period of time would make obvious to the reader certain subtle but significant shifts in the methods of communicating, in the power structures of the group, in the foci of discussion, and in the general atmosphere of the meeting. If the reader, in addition to perceiving the situation complete with its inherent interactions, tensions and problems, was aware of the therapist's theoretical orientation, he would have a clear picture of what took place in the program of group psychotherapy with narcotic addicts.

Theoretical Orientation

Group psychotherapy is a process in which people share their feelings with a therapy group. The group, in turn, reacts to expressions of its individual members and, through a system of "social feedback," provides a receptive audience which reinforces or resists the individual's expressions. The therapist's role in the group is to facilitate communication by recognizing and neutralizing impediments to communication and to reinforce the positive aspects of group activity. The positive activity of the group may be described in two dimensions, each of which contain a "content" and "process" component.[18] The first dimension deals with the alteration in personality due to the "re-education" of the addict. The content of "re-education" consisted of material which would increase the factual knowledge of the individual members of the group regarding those elements contributing to their addiction. The altering of the individual member's understanding and intergration so that he learned to react to his life stresses in more realistic (healthy) ways was a function of the **process** of re-education. These two goals, increased factual knowledge and personality alteration, will be referred to as **task functions.**[18]

The second type of positive activity relatives to how the individual members were able to function as a group. Behavior which contributes to the efficient functioning of the group will be referred to as **building and maintenance functions.**

While this paper will describe the behavior of the members of the groups in terms of "task" or "building and maintenance" functions, it must be remembered that the dichotomy is an artificial one devised for descriptive purposes.

Task Functions

The task functions of the group have been described as attempts to change the individual member's factual knowledge about life and to alter his mode of responding to his life stresses. The content of the educational aspect of the psychotherapy program focused on the facts of life related to the physical, socio-economic and psychological forces influencing the addict's behavior.

The process whereby this material was presented varied, depending upon the nature of the content, the interest of the group and the materials available. Extensive use of Negro newspapers provided material for current events. Recordings and books were used to provide material on music and Negro history. Numerous films on psychology, sociology and the pharmacology of addiction were shown. A common method of presenting educational material was in the form of short oral presentations by the therapist and/or the individual group members of published material which was then followed by a group discussion.

It is felt that while it may be necessary for the addict to acquire new information for personality growth to take place, it is not sufficient. In order for the new information to be of help to the addict, the learning process must be personalized, i.e. learned in such a way as to have realistic, **personal** meaning for each member. Only then will the addict be able to integrate the new information into new behavior. The process of re-education utilizes emotional reactions of the members to problems which arise in their daily life. Such techniques as sharing both positive and negative feelings toward the educational material as well as psychodramatic interpretation of the material and the feeling which it elicits tend to make the material have personal meaning for the individual

members. For example, during one of the meetings in which the content of discussion was a history of Negro contributions to music, one of the members became enraged at a sample of "blues" being played. Material elicited during free-association which followed indicated to the author that most of the members of the group saw "blues" as a decadent expression, i.e. the hopelessness of the Negro. Further discussion focusing on the socio-economic conditions associated with the "blues period" in Negro history and the personal association of the individual members with "blues" music attempted to get them to react less irrationally to this type of music (most of the members later stated that they felt as enraged as this one member did but were reluctant to express their hostility). While no member who disliked "blues" at the beginning of therapy showed any preference for it at the end of therapy, many of the members were eventually able to differentiate between a style of music which was part of the Negro heritage and a "rocking chair philosophy of life."*

The alteration in personality involved the learning and use of new and more realistic patterns of behavior. The new behavior patterns were developed as a result of an increase in factual knowledge and experiencing new reactions to stimuli which once evoked inadequate (i.e. non-adaptive) behavior patterns. A further example was provided by another experience in the music sessions described above. The factual material which was presented (by the members as well as the author) not only included various types of music played, but Leonard Bernstein's analysis of "What Is Jazz" was examined as well as the biographies of many of the composers and artists. As a result of the therapeutic process (eliciting emotional reactions to the learning situation and utilizing the reaction of the individual and the group to bring about change in the individual), this material played an important role in personality alteration. Not only did the meaning which many of the addicts associated with "progressive jazz" become clear to the addicts and this author, but it is felt that for some of these members, the new understanding enabled them to react differently to the emotional stimulus of "progressive jazz."

Being a heroin addict not only involves injecting heroin into one's veins, but also means participation in the drug mystique. This includes the ritual of illegal traffic and use of heroin, illegal sources of income, the perpetual need to avoid detection and harrassment, the use of a special argot,[10] and listening to progressive jazz for entertainment. Progressive jazz plays an important role as one facet of the drug mystique. It is an avante garde form of art; it is the antithesis of traditional jazz in its emotional quality, and many of the progressive jazz artists are or were at one time addicted.[20] Many of the addicts stated that not only did they enjoy listening to progressive jazz while under the influence of heroin, but that listening to progressive jazz seemed to whet their appetite for heroin. Many men said: "You can't understand a junkie (addict) unless you know what it means to hustle (earn money via criminal activity), to get mellow on stuff (become narcotized) and to dig cool jazz (to understand progressive jazz)."

The Negro addict (along with the healthy Negro) attempts to destroy the stereotype of the Negro which is that of a childlike being with uncontrolled emotions, a devil-may-care attitude, and a person who reacts to life in general, and religion and music in particular, with uninhibited expression. Progressive jazz, unlike its predecessors is a restrained form of musical expression. The behavior of an audience listening to progressive jazz is subdued—almost contemplative—quite unlike that found where "Dixieland" or "Blues" are played. There is no finger snapping or foot stamping to Progressive Jazz. Not only is this form of participation "socially unacceptable" among the progressive jazz enthusiasts, but, perhaps more important, the music does not lend itself to any form of active audience participation, even dancing. The "beatnik" philosophy which is commonly expounded by the addict seems to further destroy the stereotype of the Negro created by the press, screen and

* Acceptance of a subservient role for the Negro.

radio. The addict's expression of the beatnik dogma is, "Don't react, don't feel, don't know!!" The depressant action of heroin helps the addict to escape from life to such an extent as to make any social reaction unnecessary if at all possible.

As a result of such insight added to the awareness that they were not impotent to deal effectively with their life stresses, some members expressed new reactions to hearing progressive jazz. Toward the end of therapy, one of the men said: "I still like cool jazz, Doc, but before when I heard it, it would make me think of a cool pad (apartment) and taking off (becoming narcotized by heroin) and now it just makes me want to get a date and go to the Sutherland (a jazz center in Chicago) to hear Art Blakey (a progressive jazz artist) and have a ball (good time)."

By focusing on the patients' inadequate responses to stresses in prison and in the therapy group in particular, the therapist, together with the positive emotional forces in the group (existing to some extent at all times), was able to help the patients develop more adequate ways of dealing with their problems and so accomplish a personality reorganization. Movement toward or away from the achievement of these task functions was reflected in the behavior of the patients. This behavior may be described in terms of the extent to which an individual participates constructively in the group and helps others to participate in the group. Constructive participation involves the attitude, "group therapy can help me to become healthier". This attitude is reflected in behavior which is characterized by the patients' eventual involvement in group discussions in such a way as to result in greater understanding by the individual members of their problems leading toward the development of more realistic patterns of behavior. Concrete examples of the kind of behavior which the author described as constructive and task oriented are:

1. Proposing tasks or goals; defining a group problem; suggesting a procedure or ideas for solving a problem.

2. Requesting facts; seeking relevant information about a group concern; asking for suggestions and ideas.

3. Offering facts; providing relevant information about a group concern; stating a belief; giving suggestions or ideas.

4. Interpreting or reflecting ideas and suggestions; clearing up confusion; indicating alternatives and issues before the group; giving examples.

5. Pulling together related ideas restating suggestions after group has discussed them; offering a decision or conclusion for the group to accept or reject.

6. Sending up "trial balloons" to see if group is nearing a conclusion; checking with group to see how much agreement has been reached.

Building and Maintenance Functions

Building and maintenance functions refer to those activities which transform independent, uncooperative individuals into a cooperative social unit capable of working on and achieving task functions. Building and maintenance functions progress when impediments to communication are eliminated or neutralized. They are enhanced by the individual member's ability to delay gratification of his egocentric needs so that group goals can be achieved. The ability to delay gratification of individual needs and to move from egocentric to "group centered" values is one of the criteria for improvement in therapy.

The content of the building and maintenance aspect of therapy consisted of training the members in the rudiments of group dynamics. This was done by showing the members how specific types of behavior affected communication within the group. When member "A" wished to make a point during a discussion, his method of getting into the conversation was to interrupt whoever was talking by pointing out the window to a woman passing by, which always stopped the discussion. He would then criticize the group (which by this time would be discussing various sexual aspects of the woman) for their mundane interests and reopen the topic by introducing his comments. While he was usually effective in leading the group this way, tremendous hostility was generated in the group.

Since member "A" was seen by many in the group as too powerful an authority figure upon whom to vent their aggression, scapegoating usually followed "A's" manipulative behavior. The members of the group were not aware of why scapegoating behavior took place. By encouraging the group to examine this problem, the therapist was able to get the group to see what was taking place and why they were reacting the way they did. As a result, not only did member "A" develop more constructive methods of demonstrating his leadership abilities in the group, but the members also became more sensitive to the fact that there were reasons for tension in the group that could be analyzed and prevented by them.

Making the members more sensitive to impediments to communication not only helped the group's communication process but resulted in the group functioning at a higher level, i.e. it began to assume more responsibility for its own direction and movement.

An example of the development of the therapy group into a cooperative social unit capable of constructive activity was the spontaneous assumption of responsibility for preparation and presentation of the factual material to be discussed in the session. At the end of one of the sessions dealing with the role of the church in the Negro community, the group as a whole suggested that individuals take responsibility for the preparation of the educational sessions which were to follow. Considering the scarcity of pertinent material (most of it came from the two Negro newspapers, the Pittsburg Courier and the Chicago Defender), the group did a commendable job. The topics ranged from "the church as an anti-labor weapon in the organization of the Detroit Autoworkers" to "the history of the church as a protest organization among the slaves." The therapist's responsibility during these sessions was to moderate the discussions and to help the group overcome obstacles to communication. It should be noted that not only did the therapist share with the members a gross ignorance of Negro history, but perhaps more debilitating to his role of therapist, he lacked the personal contact with current Negro problems and had difficulty in empathizing critically, i.e. understanding how the patient perceived and reacted to his unique problems as a Negro.

While this kind of responsibility was a dramatic and a major accomplishment of the group, less striking but no less significant were the manifestations of constructive behavior by individual members which contributed to the effectiveness of the group as an entity. Examples of constructive building and maintenance behavior demonstrated by the members in the course of the therapy were:

1. Being friendly, warm and responsive to others; accepting others by giving them an opportunity or recognition.

2. Sensing feelings, moods, and relationships within the group; sharing his own feelings or affects with other members.

3. Attempting to reconcile disagreements; reducing tension through "pouring oil on troubled waters" getting people to explore their differences.

4. Offering to compromise when his own ideas or status is involved in a conflict; admitting error; disciplining himself to maintaining group cohesion.

5. Attempting to keep communication channels open; facilitating the participation of others; suggesting procedures for sharing opportunity to discuss group problems.

6. Expressing standards for group to achieve; applying standards in evaluating group functioning and production.

While it is possible to describe the behavior of the members of the therapy group in terms of **Task** and **Building and Maintenance** functions to understand the process of group interaction, it is necessary to examine in some detail the effect of the content and process of therapy sessions in order to understand the impact of the therapy experience on the participants. The following section discusses the way in which the personality structure is altered by therapy.

The Dynamics of Personality Change

During the course of his life, the addict tends to develop fairly uniform patterns of reactions to situations. He tends to

avoid emotionally charged situations by ignoring them or through drug use. He is individualistic to the extent of being completely egocentric. He feels secure with his self-depreciating, impotent self-concept as it frees him of any responsibility from participation in the external world. His claim to uniqueness lies in his knowledge of, and participation in the drug mystique. Though his aspirations are unrealistic, he never has to challenge his fantasies. While we may say that these characteristics are pathological, it must be recognized that since his experiences have not changed his orientation to life, the addict's values and attitudes are "stable," i.e. resistant to change.

The process of group psychotherapy with drug addicts consists of unfreezing the adaptive patterns of the addicts, and providing him with an experience which enables him to develop adaptive behavior which is more realistic. This is accomplished by the therapist providing a stress situation from which the addict can't effectively insulate himself with his usual modes of adaptive behavior. The incarcerated narcotic addict does not initially come to group psychotherapy meetings because of any great desire to change his way of life. It appears to the author that he comes to therapy sessions at first strictly because he has nothing better to do, and going to a "bull session with a head shrinker is better than sitting on the flats (the dormitory)." Technically, we may say the addict lacks motivation to change his behavior. The general goal of the addict in jail is to "serve easy time" (stay out of trouble in jail) and to plan how to "beat the game when he gets out" (succeed in crime). He does not see any relation between his use of drugs and the rest of his life, i.e. his marginality, his inability to endure stress, or his lack of effective means of resolving conflicts. What is more important, perhaps, is that he is not interested in working with anyone to help himself or anyone else. We may therefore say that a group of disturbed individuals come together, each motivated by different needs, and all lacking motivation to change.

How can the process of group therapy and individual change be best understood? Kurt Lewin,[21] in his life-long study of dynamics, has provided social scientists with certain insights into group processes. This, together with data about the individual psychic processes of the addict and the sociological data describing the milieu from which the addicts came, enabled the author to formulate certain approaches to the treatment of group addicts who volunteered for a group therapy program at Cook County Jail.

The goal of the therapist is to help the narcotic addict change from a person who resolves his anxiety by escaping from reality through the use of heroin to a person who tries to resolve his anxiety by actively struggling to change his world where it is realistic to do so, and by learning to endure the stresses where it is not possible to avoid or eliminate them. In order to achieve this goal, the therapist must break down the insulation which the addict has built up around himself so that he feels no need to change. The therapist, once having "unfrozen" the addict, then helps him to understand the factors contributing to his dependence on addiction as a mode of adjustment. In order for the insights gained in therapy to achieve personal and lasting meaning for the patient, behavior patterns more in line with reality must be developed and reinforced. For the incarcerated addict, this may mean more participation (overt or covert) in group activity, realistic planning for his future, and struggling in a realistic way against the discriminatory practices aimed at Negroes, addicts, and participants in therapy.*

One way in which the therapist tries to unfreeze the addict is to cause the addict to focus on the contradiction between his distorted perceptions and reality. Example: Many of the addicts express a willingness to exchange an average of 2 months/year of incarceration** for the style of living available

* Participants in the therapy program were constantly harrassed by fellow prisoners and guards.

** Statistics gathered in Cook County Jail on the addict population in therapy shows an average of 2 months/year incarceration after the first conviction when the addict depends upon criminal activity as a source of income.

to them the remaining 10 months/year as criminals. At the same time, they invest a great deal of energy in insulating themselves from the stresses of prison life. Two of these stresses are the humiliation and de-humanizing experiences involved in the status of "prisoner," and the craving for heterosexual contacts. An example of prisoner status is the requirement to undress completely any time a guard asks a prisoner to do so in order that he may be searched for contraband. This may be done in the corridors or any place else in the prison. Often a prisoner feels that a guard may order him to strip just to humiliate him.

The desire for heterosexual contacts was reinforced by the fact that a window in the therapy room faced an area through which visitors passed to and from the jail. The men in therapy were able to see these men and women, and almost every time a woman passed the window the members proceeded to verbally express their desire for heterosexual contact. The therapist in these situations would focus on the apparent contradiction between their expressed acceptance of their life as addicts and their existence as inmates of a prison. Their distortions lay in their perception of the "addict-role" as a satisfactory solution to their problems. The reality was that they were not satisfied with the solution. The therapist focused on the contradiction.

Another way in which the therapist potentiates change in the addict is by providing the addict with an understanding of the social, psychological and pharmacological factors which contribute to his dependence on narcotics. This tends to break down the mysticism associated with drug use.

While factual material may appear to the reader to be rather inoccuous because of its similarity to typical educational material, it often proved to be quite disturbing. An example of the emotional impact of certain factual material was a film shown to the therapy groups describing the anti-morphine properties of nalorphin in experimental animals. While the members of the therapy group had been withdrawn from drug use for 3-6 months before seeing the film, several of the addicts reported experiencing withdrawal symptoms the evening the film was shown and many others stated that they felt ill while watching the animals in the film go through the withdrawal syndroms. Non-addicted inmates who also saw the film did not report any discomfort either during or after seeing the film. It was felt that the disturbing attribute of this film may have been its ability to act as a conditioned stimulus triggering off psychogenic withdrawal symptoms, and/or its value in counteracting the drug mystique by describing a typical aspect of drug use (withdrawl) in an objective way.

In addition to focusing on factual material, much time was spent on affective material. By affecting material, we mean the complex of factual knowledge which has been organized into interpretation of reality by the patient, complete with the feeling associated with these abstractions. This aspect of personality theory and its relation to psychotherapy has been developed by Robbins[22] and Frank[23] in their papers on the problem of consciousness. Examples of affective material discussed in therapy are: Individual attitudes towards self, other addicts or members of the therapy group, reactions to experiences in childhood, during incarceration, and during therapy, feelings of inadequacy and hostility, reaction to erotic sensation, and attitudes and reactions towards the therapist and the therapeutic process, etc.

Perhaps the most disruptive experience to the addict's escapist orientation toward life is the therapist's providing an experience in group interaction in which the patient must work with others in a situation where the goals and methods are group determined rather than individually determined.

Since the addict's psychopathology is seen as an outgrowth of, as well as a precipitator of escape from reality and flight from healthy group activity, participation in group discussions, per se, was seen as a potentially therapeutic experience. As the patient begins to respond to the needs of other individuals in the group as well as a whole, we say he is getting better since behavior takes into account the needs of others as well as

his own needs, i.e. he is becoming less egocentric.

Summary

The process of changing an addict's personality in group psychotherapy involves: 1. Increasing the addict's factual knowledge of external reality (facts of sociology, psychology and psychopharmacology of addiction); 2. The direct experience of close interpersonal relations in which behavior is always being evaluated as to its constructive or destructive character, and reinforcement of personality change in the direction of better mental health. This entire process may be examined as consisting of two kinds of successive links in a long chain. These links are: 1. The increase in factual knowledge—impersonal, theoretical and largely abstract, and 2. the changes in feeling and behavior patterns—personal, direct, and concrete, based on reality testing. By far the most important aspect of the therapeutic process is understanding changes in reaction patterns due to reality testing. This experience provides the stimulus for new learning. New facts and theories help the patient guide his actions—but it is the empirical validation of these theories that is the most crucial phase of the process. It is one thing for a member of a therapy group to think that he is accepted by the group and it is another thing to test his hypothesis by sharing some of his doubts and anxieties with the group and sensing the group's acceptance or rejection of him, his feelings, or his attempts at testing the group. Experience provides data for theories which are tested by practice. Facts and theories provide guides for the patient's behavior. If these theories are not acted on, they become meaningless to the patient. If behavior is not related to the facts of life, then it is irrational.

As each cycle of **practice—new facts and theories—new practices,** is completed, new and higher levels of awareness develop. Understanding increases. It is no accident that as the therapy group progressed, not only did the members become more sophisticated in their perceptions of impediment to communication in the group, but much more important, they **acted** in such a way as to improve communication, e.g. less cross-talk, less attention to women passing by the window, and fewer introductions of extraneous comments during intense discussions. The process, however, is never complete. As each new stage of understanding is reached, more problems come to the surface. When the problem of communication began to be resolved in the group the men started sharing more of their anxieties with the group, and the resolution of these anxieties by the group triggered the release of many more anxieties. Lest the reader says as one of the men did, "What did I need to get myself into this mess (therapy) for? I was happier before," it should be remembered that as a consequence of therapy, not only were the men better able to accept these anxieties but in addition, these anxieties were no longer as incapacitating once they were uncovered, examined and resolved.[9]

If the reader should infer that the factual knowledge — behavioral change continuum is a relative relationship—that the understanding changes and and changes in behavior brought about in psychotherapy may be considered only superficial changes if they are not practiced outside of therapy—the author would agree. The author sees psychotherapy as an application of the scientific method, as a way of validating objective and subjective knowledge. Classical psychotherapy procedures (individual and group therapy) are only special kinds of learning—unique because the patient is primarily trying to learn about himself and the learning situation appears less threatening. The author feels that the program at Cook County Jail was succesful to the extent that group meetings focused on reality problems and attention was directed toward enabling the patients to deal more effectively with their present life as incarcerated Negro narcotic addicts who were preparing to re-enter society.

Conclusion

From the above, it may be seen how the incarcerated addict in group psychotherapy is affected by the exposure to a therapeutic process. This was described in terms of participation in constructive

group activity, the alterations in feeling and behavior through the process of exposure to new information and sharing of feelings and social feedback. The efficiency of this method of rehabilitating narcotic addicts at Cook County Jail prompted Drs. Abrams, Gagnon and the author to propose a pilot study which would test in a scientific way the methods and results of such procedures in the treatment of narcotic addicts. While it is our impression that this method of psychotherapy holds promise as a therapeutic procedure with this kind of population, more data is necessary to verify the opinions of the staff who worked on this project.

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SULFUR AND DIABETES*†

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More than 80 years ago, Borelli,[1] a spa physician in Vinadio, Italy, reported the amelioration of diabetes in patients taking sulfurous baths; since that time, numerous workers have investigated the role of sulfur and sulfur-containing compounds in carbohydrate metabolism and diabetes.[2-4] It was reported, for example, that certain sulfur-containing compounds lower blood glucose in animals[5] and that diabetic patients improve following the administration of elemental sulfur, colloidal sulfur, sulfurous waters, inorganic or organic sulfur compounds by the oral, intramuscular, subcutaneous or percutaneous route.[4,6-12] The discovery that insulin contains relatively large amounts of sulfur gave impetus to these studies and led to an extensive investigation of the effects of sulfur compounds on insulin activity, on blood sugar, and on experimental and clinical diabetes.[9,13-21] In addition to insulin, there are many other active materials containing sulfur, such as carboxylase, ketoglutaric-, pyruvic-, lactic-, malic-, succinic-, and phosphoglyceraldehyde-dehydrogenases, muscle phosphorylase, aconitase, fumarase, aldolase, hexokinase, phosphoglucomutase, phosphofructokinase, catalase, ribonuclease, ATPase, coenzyme A, lipoic acid, prolactin, thiamine, and biotin. Sulfhydryl groups are essential for the conversion of actin to actomyosin and for the formation of rhodopsin.[22-29] To the extent that these and other sulfur-containing enzymes are essential for the integrity of the metabolic machinery, sulfur can be considered to be related to diabetes, even though the manner in which sulfur causes the reported decrease in blood sugar level and the alleged therapeutic effects is unknown. More recently, this field of investigation was widened further by the accidental discovery of the blood sugar lowering action of a new group of sulfur containing compounds, the derivatives of sulfonylurea.

The sulfur content of insulin and its relation to insulin activity, secretion and degradation. The insulin molecule contains 6 cystine residues.[30-32] This relatively high sulfur content has been used by Abel to follow insulin through various fractionation procedures to its final crystallization and, more recently, for the histochemical demonstration of insulin in the pancreatic beta cells, of its release following glucose infusion, its decrease following starvation or insulin administration and of its complete disappearance following treatment with alloxan.[33] However, the relation of insulin to sulfur is not limited to the presence of this element in its molecule; sulfur, in the form of sulfhydryl groups, appears to be needed both for insulin production and for its degradation. For example, cysteine, reduced glutathione (GSH) or tissue extracts rich in these substances may influence insulin output by regulating the amount of TPNH and of glucose-6-phosphate available to the B cells,[34] and may regulate insulin degradation by causing the reduction of the -S-S- groups of cystine.[15,16,35-37] The insulin-destroying effect of rat liver extracts is believed to be enhanced by two separate enzyme systems: an enzyme which catalyzes the transfer of hydrogen from reduced glutathione to insulin and which is independent of TPN, and a TPN- and DPN-dependent glutathione reductase capable of regenerating GSH after its oxidation by insulin.[38,39]

Another major site of insulin degrada-

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tion is the kidney,[40] which, like the liver, is rich in sulfhydryl groups. It has been recently demonstrated that hypophysectomy, which reduces the rate of insulin degradation **in vivo,** also reduces the sulfhydryl content of certain portions of the renal tubule,[41] suggesting that the marked insulin sensitivity of hypophysectomized animals may be related to decreased insulin degradation.[42]

The relationship of SH-containing substances to alloxan diabetes. Numerous observations suggest that the concentration of SH-containing substances may have a direct effect on the susceptibility of the organism to diabetogenic agents. For example, the injection of alloxan produces an immediate decrease in the concentration of glutathione and ergothioneine in blood,[43] in the glutathione content of liver, intestine and skin,[44-46] and, in particular, a decrease in the sulfhydral group content of the B cells[47]. A similar decrease in the sulfhydral content of blood and tissues has been noted in experimental diabetes due to removal of the pancreas and in human diabetes mellitus.[4,7,48,49] This decrease, which may be the result of a direct chemical reaction between sulfhydryl groups and alloxan, could lead to the reduction of alloxan to dialuric acid,[50-53] a substance having a much weaker, if any, diabetogenic effect[53,54] and to the concomitant oxidation of the SH- to -S-S- groups, inactivation of SH-dependent enzymes, and to the death and disappearance of the beta cells.[55-57] In agreement with this hypothesis, it has been shown that the blood -SH content is reduced following the administration of other diabetogenic materials, such as anterior pituitary preparations,[20,58,60] adrenal cortical hormones,[61,62] acetoacetate and B-hydroxybutyrate,[63] and that the experimental reduction of glood glutathione by acetoacetate,[64] ascorbic acid,[65] starvation,[66] and low cystine,[67,68] cysteine and methionine[69,70] or sodium diets[71] not only increases the susceptibility of animals to the diabetogenic action of alloxan and anterior pituitary extracts, but may render diabetogenic substances, such as uric acid, which under normal conditions do not have this action.[70,72]

In diabetes produced by the administration of ACTH or adrenal corticosteroids,[20,61,73,74] the combination of increased purine metabolism, increased production of uric acid[73,75,76] and decreased blood glutathione may result in increased susceptibility of the organism coupled with increased production of potentially diabetogenic compounds, including alloxan itself.[53,77-80] Recent observations also indicate that glucagon, which under certain circumstances may exert a diabetogenic effect,[81-83] causes a significant decrease in the glutathione content of rat liver and blood.[84,85] Conversely, the administration of reduced glutathione produces a temporary, but dramatic amelioration of hyperglycemia and glycosuria in normal subjects treated with ACTH[86] and protects laboratory animals against the diabetogenic action of alloxan.[53] Protection against the effects of alloxan and other diabetogenic agents has also been obtained by using other means of raising blood glutathione concentration or of preventing its decrease. Among these are the administration of sodium nitrite and para-amino-propiophenone,[87] glucose cycloacetoacetate,[88] glucose, mannose or fructose,[89] cysteine or BAL,[90,91] thioglycolic acid,[92] thioctic acid[93] and other SH-compounds,[8,10,94,95] thiouracil[4] and propylthiouracil[96] or thyroidectomy.[4] It is interesting to speculate that the resistance of guinea pigs and of certain strains of mice to the diabetogenic action of alloxan may be due to their relatively high blood glutathione levels,[97-99] and that alloxan-diabetic rats which, when given a free choice of foods, consume considerably more protein than healthy controls,[100] may do so because of an instinctive craving for sulfur-containing amino acids.

The possible role of sulfur-containing compounds in diabetic complications can only be surmised, at the present time. Sulfur is part of the molecule of mucopolysaccharides and the metabolism of these substances is altered in diabetes.[101] Heparin, a sulfur-containing mucopolysaccharide, through its effects on blood clotting and on the plasma lipoprotein pattern[102,103] may be related to diabetic vascular disease. Cysteine and reduced glutathione inhibit the production of

steroids by rat adrenals **in vitro**[104] and high adrenocortical activity, which is accompanied by a decrease in blood glutathione, by an increase in uric acid and by changes in mucopolysaccharide metabolism,[105] has been implicated in the pathogenesis of diabetic retinopathy[106] and nephropathy.[107] Finally, it should be noted that high uric acid levels are sometimes associated with vascular disorders.[108]

The sulfonylureas and their mode of action. Among the sulfur-containing substances used in early therapeutic attempts are the 4- and the 5-methyl-thiolimidazoles.[109] These are closely related chemically to p-aminobenzensulfamido-isopropyl-thiodiazole (IPTD) whose hypoglycemic properties, accidentally discovered by Janbon and his collaborators,[110] led to the synthesis of the sulfonylureas now commonly used as oral antidiabetic agents. The history, mode of action, therapeutic effects and clinical indications of the sulfonylureas have been the object of a recent review[111] in which the following tentative conclusions were reached: 1) that the sulfonylureas stimulate the release of insulin from the pancreas; 2) that they suppress liver glucose production, and 3) that this hepatic action is possible only when insulin is injected, secreted spontaneously by the pancreas or caused to be released in "permissive" amounts by the drugs themselves. This hypothesis would explain why the drugs cause hypoglycemia in the absence of the liver, when glycogenolysis is absent, insulin secretion normal and insulin destruction normal or reduced and why they are not effective in the absence of functioning pancreatic tissue or of exogenous insulin and in cortisone-treated animals[112] when glycogenolysis and gluconeogenesis proceed at an exaggerated or overwhelming rate. Thus carbutamide, tolbutamide, and chlorpropamide may exert their hypoglycemic effect only in normal, partially alloxanized, partially or recently depancreatized animals, or in mild diabetic patients where some residual insulin may be present or where insulin may be provided by the stimulation of the beta cells in quantities sufficient to make the liver action of the drugs possible. Essentially the same conclusions were reached recently by other investigators.[113] They do not preclude the possibility of other mechanisms such as inhibition of insulinase activity and of insulin destruction.[114]

If this hypothesis is correct, prolonged therapy with sulfonylurea-like drugs should be attempted with caution, for the suppression of hepatic glucose production may be a sign of injury and, although continued stimulation of the beta cells may result in hypertrophy, increased insulin production[115-119] and the amelioration of diabetes,[120] it may lead also to functional insufficiency. That this may happen is suggested by the fact that pre-treatment with tolbutamide renders the pancreas unable to respond to further stimulation,[121] potentiates the action of alloxan[122] and other diabetogenic substances,[123] and, if prolonged, causes a decrease in glucose tolerance[117,123] and a gradual increase of fasting blood glucose to diabetic levels.[124,125] This important problem was investigated recently in two laboratories, including our own, using rats given a dose of alloxan sufficient to impair their glucose tolerance without causing fasting hyperglycemia and glycosuria. One group of investigators[123] found that when these "subdiabetic" rats were fed tolbutamide for a long period of time, their tolerance for carbohydrate became progressively worse, although the animals never became frankly diabetic. In our laboratory[126] chronic tolbutamide[5] feeding caused a temporary impairment of glucose tolerance which, however, returned to the initial values after continued treatment for 12 to 15 months. At this time, histological examination of the pancreas revealed the presence of numerous islets of Langerhans rich in beta granulations. On the other hand, the glucose tolerance of control sub-diabetic animals receiving no drug continued to degenerate and, at the end of the experiment, their pancreatic islet tissue was poor in beta granules. The difference between control and experimental animals was marked and significant, confirming the observation of others[127] and suggesting that the possibility of causing significant functional damage to the pancreas by

continuous sulfonylurea treatment is remote and that the drugs may actually stimulate functional regeneration. This encouraging conclusion does not eliminate the possibility that harm may be done to the patient by withholding insulin therapy; the problem of diabetic complications has not been solved, as a disturbingly large number of patients still suffer from neuritis, retinitis, lens opacities, glomerular and other vascular lesions.[128] Are these lesions related to the alterations in carbohydrate metabolism, to the disturbed lipid and lipoprotein composition of the serum, or to other unknown factors? We do not know the answers to these questions, but we do know that the major metabolic defects of diabetes can be corrected to a great extent with insulin. It is doubtful whether the same goals can be reached with the sulfonylureas which do not appear to stimulate glucose utilization directly, which may[129-131] or may not[132] correct the blood lipid aberrations and, at least in obese-hyperglycemic mice, may actually increase serum cholesterol concentration and total liver cholesterol content.[125] For these reasons, it may be wise to give the patients the benefit of the doubt and use oral therapy only as an adjuvant to insulin[133-137] or in those patients who cannot be treated with diet alone, who refuse insulin or for whom the use of insulin is made hazardous by physical or mental handicaps.

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HYPERTENSIVE CARDIOVASCULAR DISEASE AND ITS EXPERIMENTAL COUNTERPARTS*

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In the quest for improved drugs for the treatment of essential hypertensive disease, investigators in this field have faced the problem of trying to develop an experimental counterpart to what is, by definition, a group of human diseases of unknown cause. Although this is obviously an impossible task, some headway has been made in the past few decades, and it seems worthwhile to examine cursorily some of the progress today.

In order to forestall semantic difficulties, we should first agree on terminology. Hypertension means high blood pressure, and this may be considered clinically normal or abnormal in any given case. When an elevated blood pressure is a salient feature or symptom of a disease state, it can be considered abnormal and we may speak of a "hypertensive disease". There are many diastolic hypertensive diseases, and when we have eliminated the minority thereof for which the pathogenesis is proven, we are left with what is probably a heterogeneous group of conditions lumped under the heading of "essential hypertensive disease". For convenience, however, I shall follow the custom of referring to this group as "essential hypertension". I mean to emphasize that high blood pressure is most probably a symptom of essential hypertension and not the basic cause of the disease, although there certainly has been disagreement on this point in the literature.

Types of Human Hypertension

We may begin by classifying some of the diastolic hypertensive diseases of man as follows:

1. Primary renal diseases,
2. Endocrine diseases,
3. Of unknown cause (essential").

An elevated blood pressure may often accompany primary renal diseases such as obstructions to the flow of blood to the kidney and various types of nephritis—especially pyelonephritis—although hypertension is **not** an obligatory feature of renal disease. It is probably a secondary reaction resulting from activation of the so-called "renal pressor system." In this system, the enzyme renin is released from the kidney to act upon the plasma substrate, an alpha-2-globulin called angiotensinogen, which is thereby converted to the decapeptide angiotensin I and thence enzymatically to angiotensin II, and octapeptide of proven structure that is known to have a greater pressor potency than epinephrine. Angiotensin II is destroyed by a ubiquitous angiotensinase. Recently, attention has again been called to the renal juxtaglomerular apparatus as a possible anatomic site for the production of renin, primarily because the apparatus becomes degranulated in experimental hypertensive states.

Renal hypertension has a long history marked by several outstanding contributions: the disease was first noted by Bright 123 years ago; renin was discovered 61 years ago by Tigerstedt and Bergman; experimental renal hypertension was developed 36 years ago by Goldblatt; and angiotensin was synthesized just 2 years ago by Bumpus and co-workers. You will probably recognize that the term angiotensin is synonymous with the older terms "hypertensin" and "angiotonin". This substitution resulted from a recent agreement between the two independent discoverers of the substance, the late Braun-Menendez of Buenos Aires and Irvine Page of Cleveland.

The second group of diseases in our classification is termed "Endocrine" because of the known or suspected pathogenetic role of hormones. Phaeochromocytoma is a relatively rare type of

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tumor of the adrenal medulla resulting in a paroxysmal hypertension that is obviously due to the increased circulating amounts of epinephrine and norepinephrine. Hyperactivity of the adrenal cortex may cause either of two types of hypertension: Cushing's disease or primary hyperaldosteronism. Correspondingly, hypotension is characteristic of Addison's disease. Thus, either the adrenal medulla or cortex can initiate a type of hypertensive disease. Toxemia of pregnancy might also be listed as an endocrine hypertensive disease, although little of certainty is known regarding its pathogenesis.

Unilateral renal disease and these endocrine diseases are often curable (if diagnosed before irreversible changes have occurred) by simply removing the offending organ. Unilateral nephrectomy, adrenalectomy, and even hypophysectomy have been employed with success.

What now remains in our classification is termed "essential hypertensive disease". There are schools of thought that would place essential hypertension under the grouping of renal or endocrine diseases, depending upon the individual protagonist's theory. This will be evident as we explore some of these theories.

Etiology

The first suggestion, that of a primary renal lesion, is championed by Goldblatt[1]. He maintains that the initiating factor is a renal lesion, probably demonstrable histologically, although the lesion could conceivably be biochemical. This lesion activates the renal pressor system and angiotensin elevates the blood pressure. Sustained hypertension, in turn, aggravates the renal lesions, which completes the co-called "viscious circle." The adrenal cortex, in all probability, contributes also. Goldblatt marshals much evidence in his favor, such as the recent interesting clinical reported by Merrill of Boston[2]. In this case, a healthy human kidney was transplanted to a twin brother having bilateral renal hypertensive disease. The blood pressure remained elevated until the subsequent removal of the diseased kidneys, and with them, presumably the source of the renin.

Other evidence includes the finding of increased angiotensin levels in malignant hypertensive patients by Kahn and co-workers[3]. Goldblatt's position is a difficult one from the logical point of view, for it is impossible to prove that renal lesions do **not** initiate essential hypertension. On the other hand, the Goldblatt hypothesis could be tested if there were available a chemical means for blocking the renal pressor system; in whomever this reversed the hypertension, we could then conclude that we were dealing with a Goldblatt type. Such a chemical means could involve either an anti-renin for humans, similar to that employed by Wakerlin in dogs[4], or perhaps a synthetic chemical antagonist of angiotensin.

The second suggested cause of essential hypertension is that of Grollman[5,6], who maintains that there is some mechanism in the kidney that secretes a substance that **prevents** the elevation of blood pressure. This hypothesis is based upon the fact that bilateral nephrectomy results in malignant ("renoprival") hypertention; obviously, this disease cannot be caused by renin. In addition, Grollman claims to have extracted this "normalizing substance" from the kidney and to have produced antihypertensive effects following oral administration. Unfortunately, these observations have not been widely confirmed. Nevertheless, if renoprival hypertension is such a deficiency disease, this can still not negate the proofs of Goldblatt, Wakerlin, and others that renal hypertension is caused and maintained by the renal pressor system. Again, by logic, it is impossible to prove that renoprival hypertension is not caused by the deficiency of some substance. Until the time that Grollman's suggestion is proved to be true, most workers generally prefer to consider the cause of renoprival hypertension as unknown.

A third theory is really no attempted causal explanation at all, but merely the inclusion by Selye of hypertensive disease in his theory of the General Adaptation Syndrome[7]. In essence, he feels that the body maladapts to the stresses and strains of everyday living, which then results in a derailment of the nor-

mal interplay of such general hemostatic factors as the nervous system, the pituitary-adrenal system, electrolyte metabolism, and so forth. The end product is high blood pressure and pathological lesions in the cardiovascular system. These concepts have been of great value in stimulating and directing new lines of research in the field.

A more specific suggestion has been made by Raab[8]. He proposed that the reactivity of the arterioles to the catecholamines released at the sympathetic nerve endings is heightened by an increase in intracellular sodium, and that the latter, in turn, can be caused by hypersecretion of adrenal mineralocorticoids such as desoxycorticosterone or aldosterone. In the diagram below, the injection of norepinephrine or a deficiency of o-methyl transferase adds to the stimulus from the right and thus raises blood pressure; the reverse follows sympathectomy or the administration of drugs that diminish sympathetic activity. The stimulus from the left is intensified by adding a dose of a mineralocorticoid or supplying an excess of sodium, both of which supposedly increase intracellular sodium and thus increase the sensitivity of the arteriole to norepinephrine, which results in a rise in blood pressure. The reverse follows adrenalectomy, salt-free diets, or treatment with natriuretic agents.

ADRENAL CORTEX	CORTICOIDS	ARTERIOLE (Na^+)	NOR-EPINEPHRINE	SYMPATHETIC SYSTEM
	——————>		<——————	

It has been demonstrated fairly consistently that vascular hyper-activity actually does occur in experimental and human hypertensive diseases of various types, and Mendlowitz[9] has recently suggested that the hyper-reactivity in essential hypertension might be caused by an inability to destroy norepinephrine as a result of o-methyl transferase deficiency.

Irvine Page, who has done much to bring lucidity into this field, has deplored the tendency to ascribe essential hypertension to any sole pathogenetic factor[10]. He prefers to think of the hypertensive process as an equilibrated system in which one of several different pressor mechanisms may predominate at any given time. However, our goal must be to discover what **initial** sets of conditions can serve as the basic cause of each type of essential hypertension and to direct therapy at correcting or preventing this condition. With the statement of this goal, let us now consider some of the various types of experimental hypertension that have been studied and what knowledge has been gained.

Experimental Hypertensions

Paralleling somewhat the types of diastolic hypertensive diseases found in man, we may classify the major types of experimental diseases as (a) renoprival, (b) renal, and (c) endocrine.

Renoprival hypertension we have mentioned before in connection with the Grollman hypothesis. Following bilateral nephrectomy, there is usually an expansion of the extracellular fluid volume, although it has been shown that the hypertension and arterial necrotic lesions can occur even if the fluid volume and electrolyte balance are maintained at seemingly normal levels. Nephrectomized, hypertensive animals have been maintained for many months by parabiosis, repeated peritoneal lavage, or use of the artificial kidney. The absent excretory function of the kidney is not fundamentally involved, because hypertension does not follow the implantation of the ureters into the vena cava. Most investigators feel that sodium and the adrenal cortex play an important role, although there is no general agreement on what this might be. Renoprival animals do display vascular hyper-reactivity and it is conceivable that this is caused by an intracellular shift of sodium. Such a shift may well be of a magnitude too small to measure. This is really a way of saying that we are essentially ignorant of the cause of renoprival hypertension. Pathologically, animals with this disease have been likened to patients having malignant hypertension.

Renal hypertension results from inter-

ference with the kidney and is caused by activation of the renal pressor system. The disease is often called "Goldblatt hypertension" in honor of the man who first produced it with predictable regularity in dogs. Common means for initiating the disease include clamping the renal artery, partially ligating the aorta cephalad to the renal arteries, and inducing perinephritis by wrapping the kidney with an irritating material. It is not necessary to cause renal ischemia. If only one kidney is manipulated, only the contralateral kidney develops the sclerotic and hyalinized lesions. (This is one of the arguments of those who claim that an elevated blood pressure per se causes vascular lesions.) Cardiovascular hyperreactivity is present. Since anti-renin reverses both acute and long-standing experimental renal hypertension, there does not seem to be any question as to the role of renin in causing and maintaining it. Again, other hormonal substances play a permissive role. Hypophysectomy, for example, cures the disease and adrenalectomy often has an ameliorative effect. Since renal hypertension or the injection of renin results in hypertrophy of the zona glomerulosa, it is quite possible that a secondary adrenal-type of hypertension ensues. As mentioned earlier, the question of similarity of renal to human essential hypertensive disease will have to await the availability of human anti-renin or anti-angiotensin drugs.

The last major type of experimental hypertension I shall consider is what we may call the "endocrine type". Several main subdivisions can be distinguished. Sodium, or salt, hypertension is easily induced in rats by feeding them diets containing 2% or 3% salt. After a month or so, the animals display a well-defined hypertension and cardiovascular lesions. If, however, the high salt diet is then removed, these changes soon disappear. It is conceivable, however, that if rats were to be maintained on these high salt diets for a prolonged period—say a year or more—that an irreversible stage of hypertensive disease could be achieved. Such an experiment has not yet been reported. Nor has anyone investigated the possibility of similarly producing sustained salt hypertension in dogs, a species notably more resistant to the pressor effects of sodium. The experiment may well have been performed by Nature in humans, however. Kohlstaedt and co-workers have been studying hypertensive individuals in the Bahamas[11]. The drinking water there was found to contain upwards of 2 gm. of sodium per liter (as compared to 0.3 in New York and the native diet consisted mainly of foods fried in salt pork oil containing large amounts of sodium. Under these dietary conditions, polydipsia was common and some 65% of the population studied exhibited a degree of diastolic hypertension. These findings are certainly suggestive and further reports will be received with great interest.

The second type of endocrine hypertension is that produced in rats by desoxycorticosterone acetate (DCA) implantation and normal saline for drinking fluid. Many investigators also remove one kidney. The hypertensive disease that results is characterized by polydipsia, polyurea, exaggerated excretion of a sodium load, vascular lesions and hyperreactivity, cardiorenal hypertrophy, nephrosclerosis, and decreased life expectancy. Apparently DCA hypertension is an accelerate and exaggerated form of sodium hypertension. It is easily produced in rats, but in dogs only with difficulty. In man, the pressor effectiveness of DCA in Addisonians is well-known.

As one might predict, glucocorticoids such as cortisone and cortisol are also capable of producing hypertensive disease in rats. In this instance, though, we do not have a simple case of aggravated sodium hypertension, for the disease cannot be induced in rats receiving a high salt diet, but only in those on a low or normal salt intake. The reason for this is not known, and the finding was somewhat surprising, especially since the difference between mineralocorticoids and glucocorticoids is not one of kind, but one of degree.

With the discovery of aldosterone, it was thought that this agent might be much more potent than DCA in producing experimental hypertension. However, it soon developed that aldosterone was a less potent pressor agent than DCA, when given in equivalent sodium-retaining

doses. Nevertheless, Skelton[12] felt that hypertension might result if the adrenals could be rendered hyperactive in some way. He discovered that, if rats were given normal saline to drink and subjected to uninephrectomy, uniadrenalectomy, and contralateral adrenal enucleation, then the regenerating adrenal glomerulosa was accompanied by a developing hypertensive disease not unlike that caused by DCA. Since others had previously considered the glomerulosa as the site of production of mineralocorticoid hormones, the conclusion seemed inescapable that Skelton's "adrenal regeneration hypertension" was due to excess aldosterone secretion. However, adrenal venous chromatograms subsequently demonstrated that steroid hypersecretion did not occur during regeneration. Thus, we are currently left with the hypothesis that the temporary period of adrenal insufficiency somehow sensitizes the animals to the hypertensive action of the steroids secreted by the regenerating adrenal.

Last, but not least, we come to metacorticoid hypertension, a self-sustaining disease that is initiated by administering a DCA pellet and replacing the rats' drinking water by normal saline[13]. A hypertension ensues that becomes, in a few months, independent of the inciting factors. In other words, if the DCA remnants are removed and the saline replaced by tap water, the disease continues unabated. A possibly similar phenomenon occurs in adrenal regeneration hypertensive rats and there are recent suggestions that high salt diets alone might produce a sustained hypertension in rats. Remembering that experimental hypertension produced by the glucocorticoids is not sodium dependent, it is of interest that the several attempts to produce a sustained or metacorticoid hypertension with these steroids have met with failure.

In the temporal development of metacorticoid hypertension in rats, the period of DCA absorption is associated with a rapid elevation of blood pressure and a high mortality rate. When the absorption of DCA ceases or the pellet is removed, the blood pressure is maintained at a high level and the mortality rate decreases. Rats in this metacorticoid state display a great exaggerated urinary excretion of sodium following an imposed load; there is also vascular hyper-activity to norepinephrine and other pressor agents. Both of these findings have been repeatedly made in human essential hypertension as well.

With regard to the central nervous system, we have recently discovered that the electroshock seizure threshold, which is elevated in rats by DCA plus sodium, apparently reverts to normal in the metacorticoid stage. While the anticonvulsant effect of DCA is thought to be associated with **decreased** brain intracellular sodium, the pressor effect of DCA is probably related to **increased** arteriolar intracellular sodium. Perhaps the shift in the brain is reversible, while the shift peripherally is not.

A very important etiologic consideration is the fact that some metacorticoid rats can develop hypertension, lesions, or excess fluid exchange in the absence of one or both of the other symptoms. This fact led us to ascribe the basic cause of these outward symptoms to some earlier, more fundamental disturbance, possibly in cellular electrolyte metabolism. By extension, we may ask if one cause of human essential hypertension may not lie in the same direction?

Metacorticoid hypertension is not dependent solely upon electrolyte and nervous participation, for investigations on the endocrine system in particular have revealed several "permissive" mechanisms that are necessary for the production and maintenance of the disease. These include the functions of the pituitary, thyroid, and kidney.

We have increasingly felt that essential hypertension is simulated most closely, in its physiologic, pharmacologic, and anatomic characteristics, by the metacorticoid syndrome. We certainly do not feel they are identical, of course, but they appear similar enough to warrant studies on the one as a means to the eventual clinical treatment of the other. Unfortunately, only one treatment has so far **cured** hypertensive disease, this being hypophysectomy, which we feel is not likely to be reduced to routine office practice in the near future.

There is one more major point that

I should like to emphasize. In **any** form of experimental or human hypertensive disease, the initiating factor merely serves to set into motion a sequence of events in which other, secondary factors come to contribute. This results in an interplay of factors that serve to render the disease self-perpetuating. For example, an initial renal hypertension in all probability causes a secondary adrenocortical hypertensive reaction that is imposed upon the original renal one. Similarly, an initial adrenocortical hypertension probably activates secondarily the renal pressor system. And both renin and the adrenal cortex exert significant effects on water and electrolyte metabolism. While it is quite proper to speak of a single initial cause of a hypertensive disease, with time there are many things contributing to its progress and, in fact, the original cause may eventually no longer be present. Therefore, it is unreasonable to speak of a single pathogenetic factor in the maintenance of established hypertensive disease. And who knows but what the disease becomes established **before** the blood pressure begins to increase?

In closing, we may ask: What are the salient problems in the realm of hypertension that can profitably be investigated by the future study of experimental counterparts? To list a few of the more important ones, the fundamental role of the sodium ion, and the mechanism by which the sino-aortic barostats become reset at higher levels. As mentioned earlier, we must also elucidate the cause of renoprival hypertension and the role of the renal pressor system in non-renal hypertensions. These are but a few of the interesting challenges that lie before us. We may sincerely hope that concentrated investigative efforts on these and other questions will, within the not too distant future, relegate human hypertensive diseases to those disorers completely susceptible to medical management.

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RADIATION PNEUMONITIS: A CASE REPORT

ROBERT SIMON, M.D.*

Radiation pneumonitis may occur during or after radiation therapy of intrathoracic or extrathoracic disease. It has most often been reported complicating the irradiation of carcinoma of the breast, but it also occurs as a result of irradiation of lymphomas, carcinoma of the lung and esophagus, and following the treatment of pulmonary metastases of carcinoma of the thyroid with radioactive iodine.[1,2] The incidence of radiation pneumonitis is in doubt, but there has been an increase with the corresponding improvement in the technique of administration of larger tumor doses in deep radiation therapy.[3] In irradiation for carcinoma of the breast, the rate of occurrence has varied from 6% to 22-60% depending upon the method of therapy, either the tangenital or the direct portal technique. The incidence of symptomatic pneumonitis correspondingly has ranged between 1% and 18%.[4] Similar figures are reported for carcinoma of the lung and esophagus though the series quoted are generally small. The major therapeutic agents of benefit at the present time are the steroid compounds, but their effectiveness is limited[1]. The following is a report of a patient believed to have radiation pneumonitis following therapy for carcinoma of the lung and for which steroids were administered.

CASE REPORT

The patient is a 61 year old caucasian male who was admitted to the West Side Veterans Administration Hospital for the first time in July, 1959. He related a history of chronic bronchitis of some 40 years duration with progressive exertional dyspnea of two years duration. He had smoked up to two packages of cigarettes a day for 20 years but had stopped smoking 10 years prior to admission. .He was admitted in moderate respiratory distress, febrile, and cyanotic with physical findings compatible with an acute pneumonitis of the right lower lobe. A roentgenogram of the chest revealed a large patchy opacity of the right base and increased hilar shadows on the right. (Fig. 1) The patient exhibited a satisfactory clinical response to tetracycline and supportive measures, but the hilar area of opacity cleared only minimally. Fig. 2.) Further work-up included bronchoscopy which revealed a large mass extending from the basilar lobe orifice on the right side. The mass was biopsied and the pathological diagnosis was that of a small cell carcinoma. The patient initially refused any treatment but subsequently consented to radiation therapy as an out patient. He received 4080 R through 4 ports over a 49 day period. During this time, the tumor mass markedly decreased. (Fig. 3) Firm cervical nodes, which had appeared toward the end of therapy, responded to a dose of 450 R.

In November 1959, one week after his last radiation treatment, he was readmitted with fever and a productive cough of two weeks duration. He was poorly nourished, moderately dyspneic, and exhibited a prominent abdomen. His temperature was 102°; pulse 120; blood pressure 120/80. There was minimal cyanosis without clubbing. Hard supra-clavicular nodes were palpated on the left side. The chest moved poorly with respiration. Tactile and vocal fremitus were equal bilaterally. Sub-crepitant rales and expiratory wheezes were heard over the right lower lung field. Pigmentary changes secondary to irradiation were present on the anterior medial chest wall and right para-vertebral area. The hemogram initially revealed a white blood count of 3,750 cells with a differential of 88 neutrophils, 14 lymphocytes, 1 monocyte, and 1 basophil; hemoglobin 12.5 gms.; hematocrit 40%. A roentgenogram of the chest at this time revealed an irregular linear opacity having the appearance of an "infiltrate" occupying most of the

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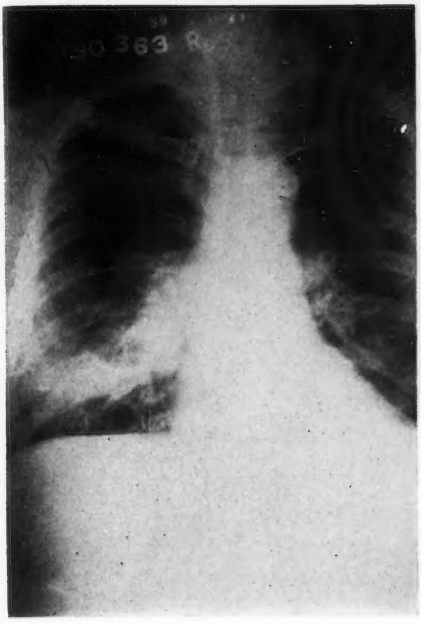

FIGURE I

Patchy opacity of right base and increased hilar shadows on the right side.

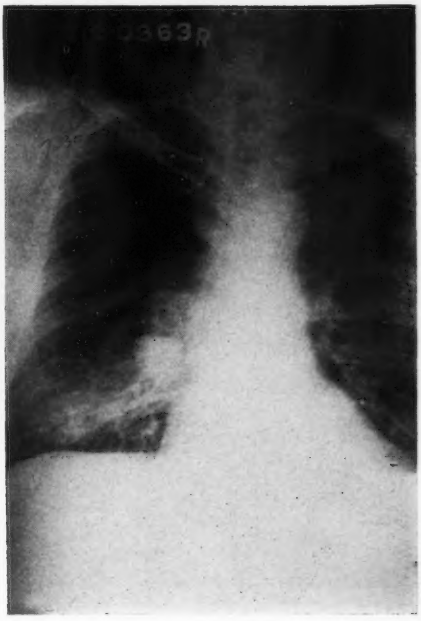

FIGURE II

Minimal clearing of opacity of right hilar area and lower lung field in response to tetracyclene and supportive therapy.

right lung field. (Fig. 4) This was not present previously. Sputum cultures showed growth of alpha steptococci, pneumococci and staphylococcus areus—coagulase positive, all of which were sensitive to penicillin, tetracycline and other antibiotics tested. The electrocardiogram revealed a right bundle branch block (present prior to radiation therapy) and premature auricular beats. The patient had a spiking fever to 102°. The administration of penicillin and later tetracycline produced no significant change. A white blood count during the second week of hospitalization revealed 4200 cells, with a differential of 70 neutrophils, 18 lymphocytes, 7 monocytes, and 5 eosinophils. Repeat cultures, in addition to the above bacteriology, revealed a few paracolon, pseudomonas, and aerobacter organisms.

During the third week of hospitalization, antibiotics were discontinued, and prednisone, 20 mgm. a day in divided doses, was administered. The temperature fell to below 100° for approximately 10 days. It again occasionally became elevated to 102° though not as a daily occurrence and later the patient became essentially afebrile. He was at this time producing up to 60 cc. of clear sputum per day and appeared somewhat dyspneic. There was persistent expiratory wheezing in the right chest and cough was a prominent complaint. He subsequently developed chest pain and right upper quadrant discomfort with enlargement of the liver to four fingerbreadths below the right costal margin.

During nine weeks of hospitalization the roentgenogram of the chest remained essentially unchanged. The last white blood count revealed 13,000 cells with 88 neutrophils, 14 lymphocytes, 1 monocyte, and 1 basophil.

DISCUSSION

Ionizing radiation may produce changes in all tissues through which it passes.

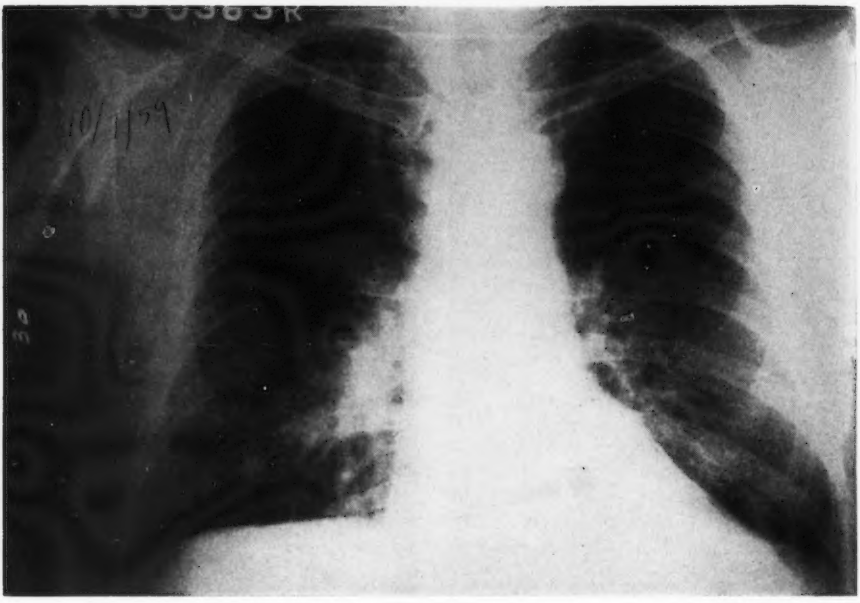

FIGURE III
Response of tumor mass to 4080 R through four ports over a 49 day period.

If the dose is sufficient, inflammation and subsequent scarring will result.[5] Different normal tissues of the body show a variable response to irradiation. The lung constitutes one of the more sensitive structures.[6] Certainly it is more sensitive than the heart. The response of the lung itself is variable and the occurrence of changes as regards time of appearance, extent of involvement and persistence of changes will differ from patient to patient.[6]

This variability in patient response is a function of two groups of factors, physical and biological. The physical factors include total radiation dose, rate of administration and the area of the lung irradiated. The biological factors include individual response to roentgen rays, age, and status of the vasculature and pulmonary parenchyma prior to therapy.[1,7] When these variable factors are considered along with the differential diagnosis of the x-ray changes seen in radiation pneumonitis which includes the possibility of tuberculosis and other infections, fibrosis from other causes, and the progression of the original lesion as in carcinoma of the lung or lymphoma, the diagnosis may be difficult.

Pathophysiology

It was in 1922 that the effects of irradiation of the lung were first sufficiently know to be published.[5] Three stages of histological change were described as the result of irradiation. The acute stage is characterized by injury to the tracheal and bronchial epithelium, the alveolar cells, and the capillary endothelium resulting in edema, lymphectasis, congestion, and minimal inflammatory cell infiltration. The subacute stage reveals diminished alveolar spaces secondary to cellular proliferation with thickening of the alveolar walls, filling of the alveoli with macrophages and the formation of a hyaline membrane. The late stage shows perivascular thickening of the alveolar walls and septa, patchy atelectasis, and pleural adhesions.[3,8]

Pulmonary function studies in these patients reveal impairment of the alveo-

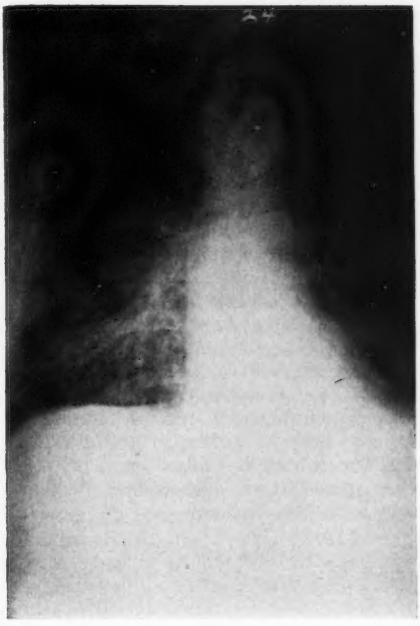

FIGURE IV

Irregular linea opacity of the right lung field—not present previously.

lar capillary oxygen diffusion rate with hyperventilation, reduced O_2 consumption with exercise, low arterial CO_2, and increased dead space.[1]

Most patients receiving radiation therapy to the thorax remain asymptomatic. Some have symptoms with minimal roentgenographic changes; others exhibit no symptoms and extensive roentgenographic findings.[6] Though clinical and radiographic findings may appear from two to six months following the last radiation treatment, the earlier the onset the more acute the clinical picture will be. Warren and Spencer feel that the acute reaction in the lung corresponds in time to the height of cutaneous changes.[5] Symptoms may vary from an occasional mild cough, slight malaise and dyspnea to an acute febrile illness with chest pain, severe, usually nonproductive, intractable cough, and marked dyspnea. The period of fever may be brief, but the pain, cough, and dyspnea may persist. The fever may be sustained or intermittent and as high as 104°. There may be associated chills. In the mild reactions, the inflammation may subside in a few weeks or months with little or no residual evidence of inflammation. In the more severe cases, however, inflammatory changes may persist for months or years with the development of cyanosis, clubbing, hemoptysis, pulmonary hypertension, cor pulmonale and death in cardiac failure or pulmonary insufficiency. On physical examination rales may be heard (dry or moist) and there may be an inspiratory "catch".[3,4,9]

The chest roentgenogram often reveals an area of increased density on the irradiated side. This density may be homogeneous, as a result of pleural reaction, but is usually irregular, patchy or linear. It may start in the hilar area and spread peripherally to involve the entire lung. The mediastinum may be displaced to the affected side and the diaphragm elevated. Diaphragmatic and pericardial tenting have been noted. Further progression reveals residual fibrosis appearing as linear, less commonly patchy, areas of density with retraction and compensatory emphysema. Bronchiectasis may be a late sequel.[4,5,10]

Neutropenia is often present early in the course. Electrocardiographic changes have been reported consisting of T wave changes, first degree block, and auricular tachycardia as well as right ventricular prominence. The etiology of these changes, however, may not necessarily be related to the pneumonitis.

Treatment

Various drugs such as heparin and dicumarol have been used with little success in the therapy of radiation pneumonitis. Some benefit with 1-triiodothyronine has been reported in radiation dermatitis, but its usefulness in radiation pneumonitis must be further evaluated.[11]

ACTH and steroids, because of their anti-inflammatory effect and clinical success in other conditions characterized by pulmonary fibrosis, have been used and appear to be the most beneficial method of treatment. Although these drugs have been found to relieve symptoms, there

is no definite evidence that they prevent or alleviate the objective signs of this disorder or increase the survival of the patient. Their greatest benefit appears to be in those patients who would otherwise survive if they could be helped through the potentially fatal acute phase of radiation pneumonitis. Subacute and chronic changes may occur despite suppression of the acute phase clinically or in the absence of an apparent acute phase.[1] The average dose of steroids used has been a 100 mgm. of cortisone or its equivalent in other steroids. With progression of symptoms, increasing doses have little effect. In general, the more prompt the administration of steroids at the onset of symptoms or occurrence of roentgenographic changes without symptoms, the more favorable the results.

SUMMARY

Radiation pneumonitis is a result of changes involving the blood vessels, connective tissue, and epithelial lining of the lungs, as well as the mesothelium of the pleura. The diagnosis is dependent upon the clinical history, the previous appearance of the lung on roentgenogram, and the development of changes on the irradiated side.[2]

The patient presented in this paper is thought to have a radiation pneumonitis in view of his clinical course, roentgenograms, laboratory findings, and lack of response to chemotherapy. There has been a minimal clinical response to steroids, and no significant change in the roentgenographic findings, although therapy has been of a relatively short duration for complete evaluation. The presence of metastatic disease may preclude long term observation.

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FLUORESCENCE SPECTRA OF 59 POLYCYCLIC AROMATIC HYDROCARBONS *

William Lijinsky, Ph.D., Anne Chestnut, B.S., and C. R. Raha, D.Phil.**

The phenomenon that many polycyclic aromatic compounds exhibit characteristic fluorescence spectra under suitable excitation enabled Hieger[1] to isolate benzo(a)pyrene from coal tar and shortened the chemical analysis. Schoental and Scott[2] have investigated the fluorescence spectra of benz(a)anthracene and a number of its derivatives. Since then, the fluorescence technique has been used to identify several polynuclear aromatic hydrocarbons in natural sources. In the case of compounds which have practically identical ultraviolet absorption spectra, for example, benzo(a)pyrene and benzo(ghi)perylene, the fluorescence spectra can be used to advantage in differentiating these compounds.[3] Fluorescence spectra provide confirmatory evidence in the identication of polynuclear hydrocarbons which often are isolated in such small quantities as to make absorption spectroscopy the means of identification.[4] Chaudet and Kaye[5] used the Beckman DK-1 spectrophotometer to record the fluorescence spectra of anthracene, benz(a)anthracene, 7,12-diphenylene(a)anthracene, benzo(a)pyrene, 3-methylcholanthrene, and dibenz(a,h)anthracene.

Of fluorescence spectra that have been published, most have appeared in the report of Van Duuren[6,7] and of Lyons and Johnston.[8] Van Duuren has published spectra of pyrene, 4-methylpyrene, benzo(a)pyrene, benzo(e)pyrene, benzo(ghi)perylene, fluoranthene, 8-methylfluoranthene, chrysene, 1,2-benzfluorene, and 1, 8, 9-perinaphthoxanthene. Lyons and Johnston have identified benzo(a)pyrene, benzo(e)pyrene, dibenz(a, i)pyrene, dibenz(a, h)pyrene, benz(a)anthracene, perylene and benzo(ghi)perylene.

The purpose of this work was to study fluorescence spectra of polycyclic aromatic compounds, some of which, it appeared, had not been investigated under the following experimental conditions. Such spectra would be helpful in the determination of trace amounts of polycyclic aromatic compounds, which has assumed importance in environmental cancer studies.

The Beckman DK-1 spectrophotometer, adjusted for fluorescence measurement, was used. Cardon and co-workers[9] have described the fluorescence attachment to the Beckman DK-1 spectrophotometer. Iso-octane solutions of the compounds were prepared having an ultraviolet absorbance at 360 mμ (presented in table 1) of not less than 0.01 with 1 cm. light path. Spectra were recorded between 370 and 700 mμ. The entire procedure was carried out at room temperature. At the concentrations specified the following compounds showed no appreciable fluorescence: Carbazole, chrysene, benzofluorenes, pentacene, picene, phenanthrene, benzo(c)phenanthrene and triphenylene. The spectra of the other compounds are presented on the following pages and are summarized in table 1.

Discussion

It is apparent that the fluorescence technique described is valuable in identifying those polynuclear compounds which have appreciable fluorescence in light from the mercury arc. In some cases the fluorescence spectra can differentiate homologs of polynuclear compounds (e.g. the methylbenzanthracenes) which are indistinguishable by means of absorption spectra. The source of the compounds is given in table 1 as L for L. Light & Co., E. for Eastman Organic Chemicals, and N. for M. S. Newman. The methods of purification of some of these compounds have been mentioned earlier.[4]

Acknowledgment: The authors thank Dr. Philippe Shubik for his advice and encouragement throughout the work.

*The nomenclature and numbering of the compounds are according to Chemical Abstracts.

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TABLE I

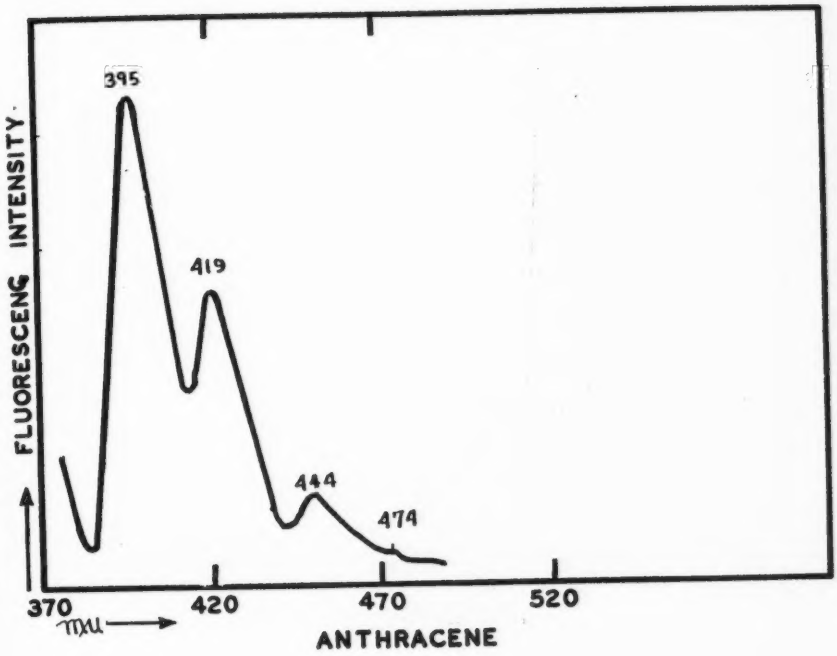
Hydrocarbon	Source	Absorbance at 360 mμ	Fluorescence Maxima (mμ)
Carbazole	L	0.0325	No fluorescence at these concentrations. Some of them can fluoresce at higher concentrations as is shown at the end of the table
Chrysene	"	0.01	
11 H-Benzo(a)fluorene	"	0.04	
11 H-Benzo(b)fluorene	"	0.04	
7 H-Benzo(c)fluorene	"	0.03	
Pentacene	"	0.045	
Phenanthrene	E	0.04	
Benzo(c)phenanthrene	N	0.095	
Picene	L	0.015	
Triphenylene	"	0.011	
Benz(c)acridine	L	0.37	385, 392, 404, 428, 446
Anthracene	E	0.02	375, 395, 419, 444, 474
1-Methyl	N	2.06	383, 400, 424, 450, 470
9-Methyl	"	---	389, 409, 434, 463
9,10-Dimethyl	Cason	6.96	405, 422, 448, 476
Benz(a)anthracene,	L	0.04	385, 407, 430, 458
1-Methyl	N	16.16	390, 410, 432, 456
2-Methyl	"	5.28	388, 409, 434, 456
3-Methyl	"	2.18	383, 395, 406, 428, 450
4-Methyl	"	7.84	387.5, 409, 432, 456
5-Methyl	"	6.68	389, 410, 434, 460

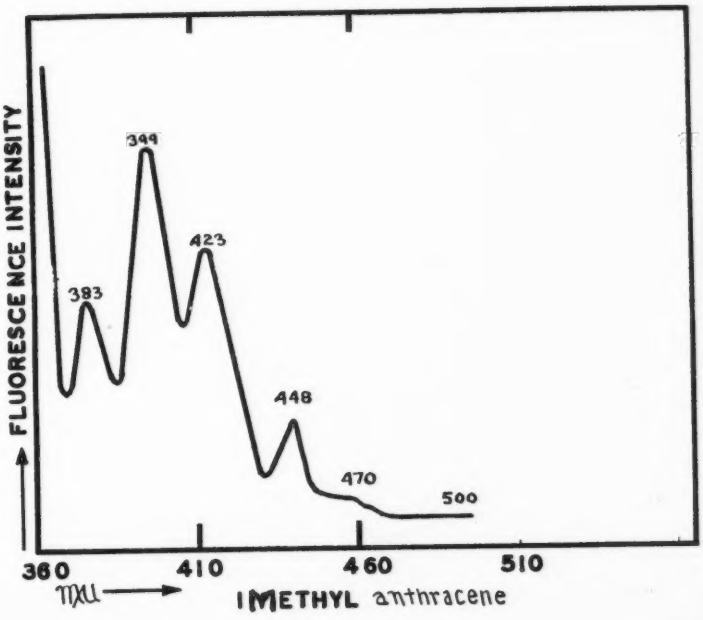
TABLE I (Continued)

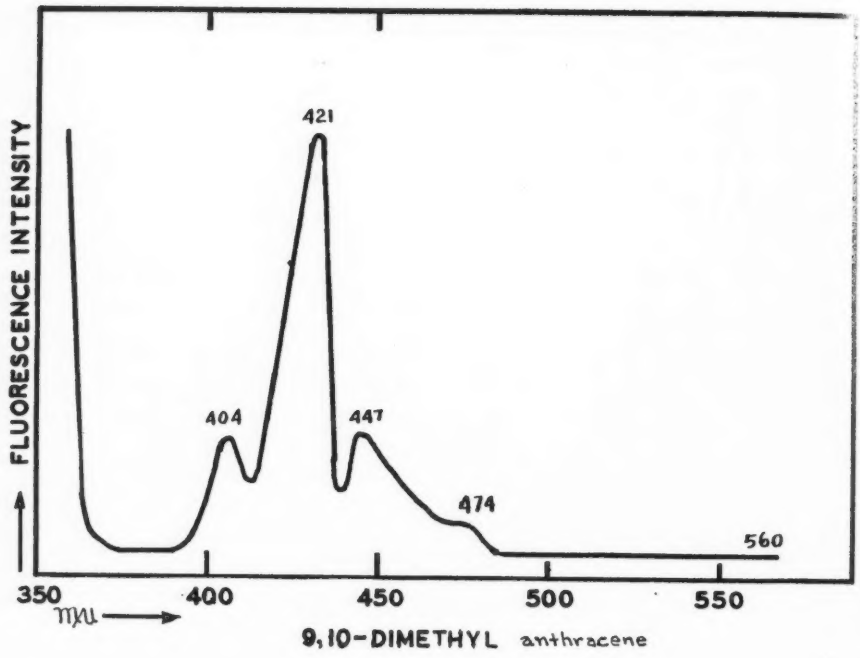
6-Methyl	N	11.52	387, 407, 431, 458
7-Methyl	"	6.08	390, 395, 412, 434, 460
8-Methyl	"	1.74	385, 407, 430
9-Methyl	"	3.4	395, 408, 432, 450
10-Methyl	"	2.74	388, 409, 433, 460, 490
11-Methyl	"	4.72	386, 407, 430, 458
12-Methyl	"	4.36	397, 416, 438
7, 12-Dimethyl	E	0.53	410, 424
3, 4-Benz	L	0.15	375, 395, 419, 444, 474
Dibenz(a, h)anthracene	E	0.02	394, 405, 414, 430, 442
Anthanthrene	L	0.045	433, 453, 482
11 H-Benzo(a)carbazole	"	0.05	406
11 H-Benzo(b)carbazole	"	0.12	408, 385
7 H-Benzo(c)carbazole	"	0.12	396
Cholanthrene, 3-Methyl	E	2.06	392, 415, 439, 466
Coronene	L	0.035	417, 440
Fluoranthene	"	0.53	438, 462, 482
Benzo(b)	"	0.28	402, 428, 448
Benzo(m.n.o.)	"	0.06	418, 444, 472, 490
Fluorene	E	0.085	397, 420
Naphthacene	L	0.02	470, 500
Perylene	"	0.15	442, 462, 494, 520
Benzo(ghi)	"	0.175	417, 440, 456
Benzo(c)phenanthrene,			

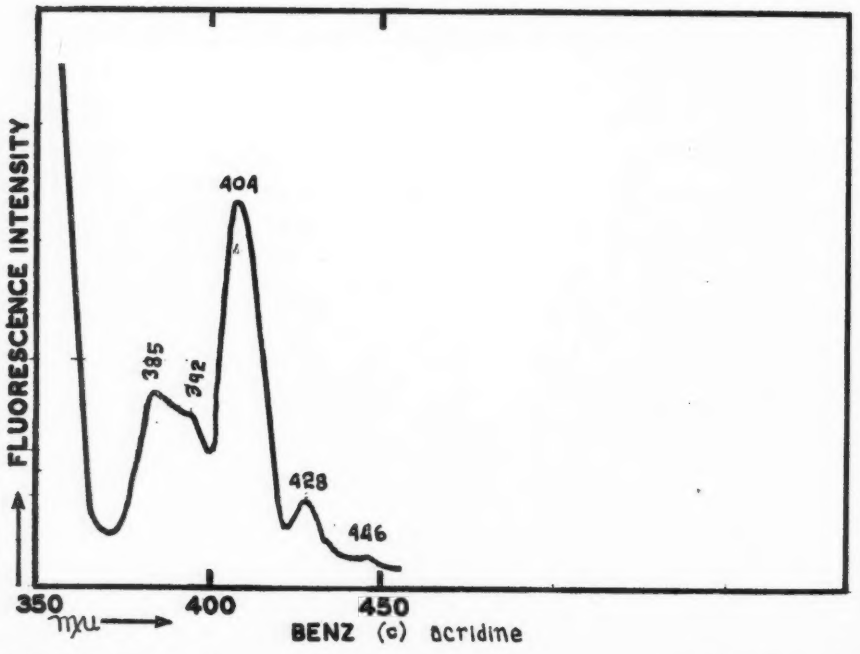
TABLE I (Continued)

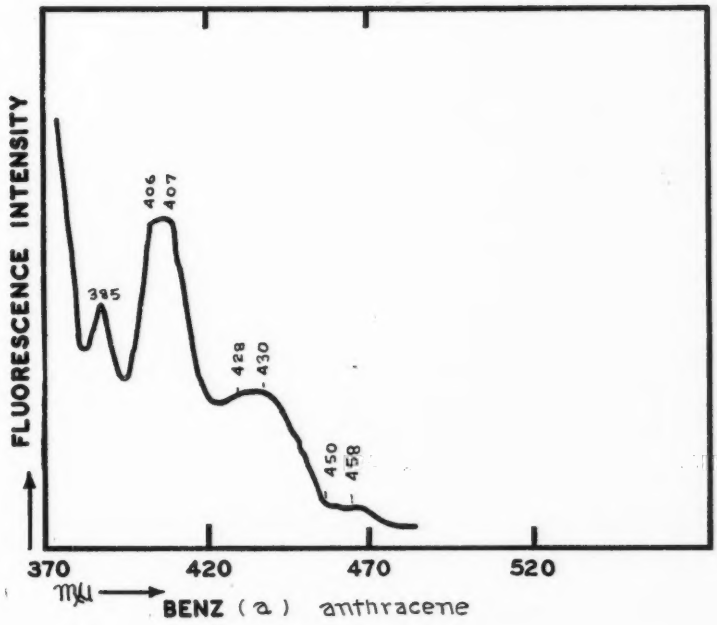
3-Methyl	N	0.18	396, 402
7-Methyl	"	1.06	400
8-Methyl	"0	0.2	396, 402, 420
9-Methyl	"	0.45	402, 422
11-Methyl	"	0.46	396, 416
12-Methyl	"	0.3	395, 410
Pyrene,	L	0.015	440, 460
4-Methyl	"	0.46	392, 412, 468
6-Methyl	"	0.09	392, 412, 468
7-Methyl	"	0.42	476
Benzo(a)	"	0.035	395, 401.5, 409, 416, 428, 450
Benzo(e)	"	0.015	410, 434, 458
Dibenzo(a, l)	"	0.39	476, 500
Dibenzo(a, i)	"	0.085	430, 453, 484
Phenanthrene	E	---	398, 420, 448
Carbazole	L	--	408, 429
Chrysene	"	---	387, 400, 408, 423, 450

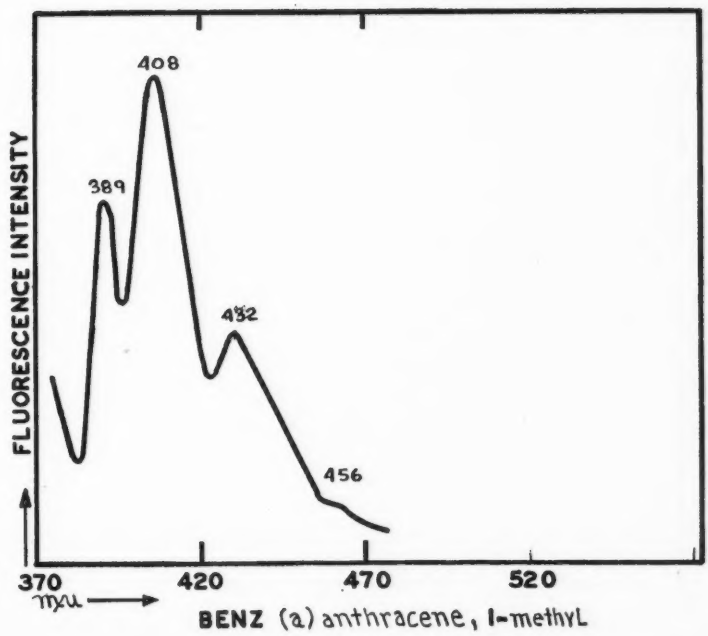

395
419
444
474
FLUORESCENG INTENSITY
370
420
470
520
mμ
ANTHRACENE

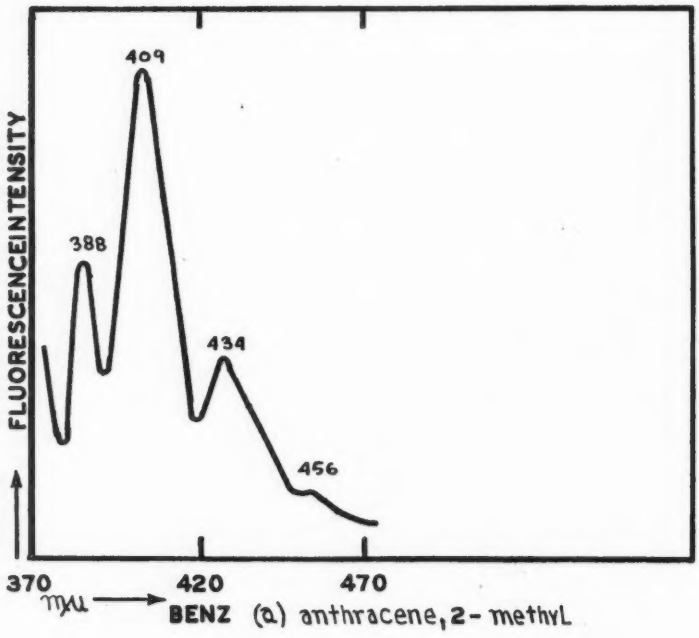

399
423
383
448
470
500
FLUORESCENCE INTENSITY
360
410
460
510
mμ
1METHYL anthracene

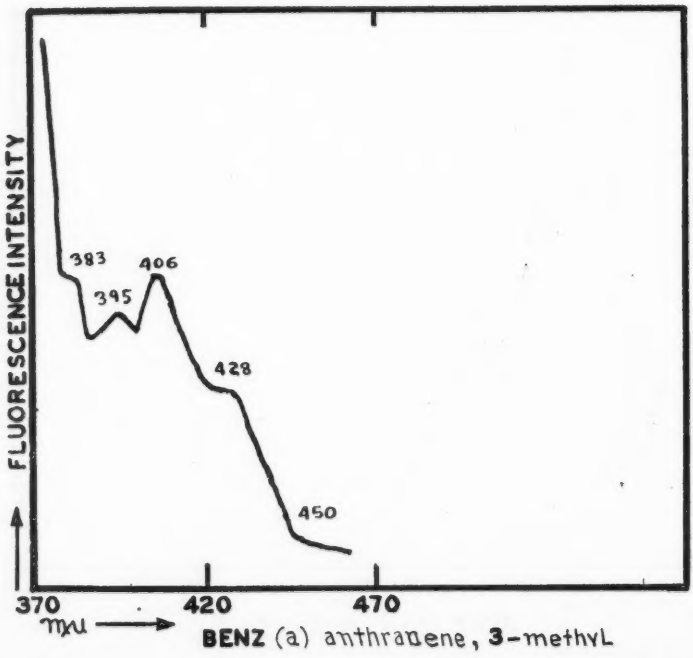

FLUORESCENCE INTENSITY
421
404
447
474
560
350
400
450
500
550
mμ
9,10-DIMETHYL anthracene

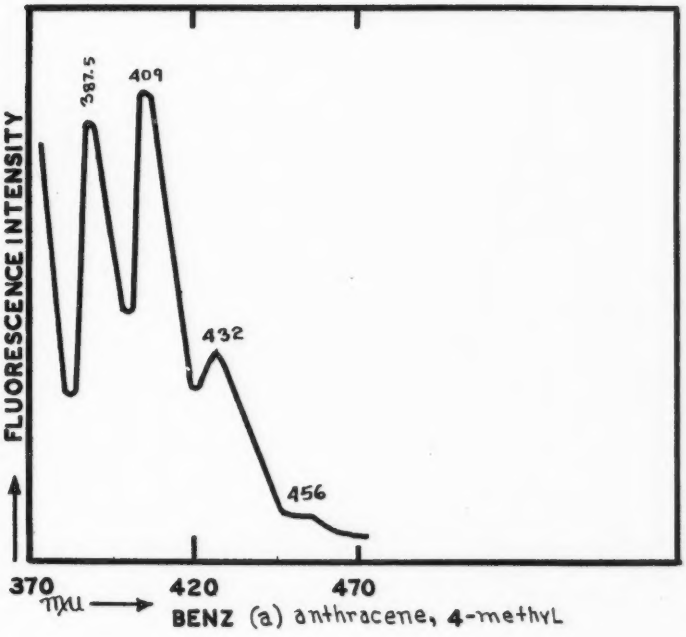

FLUORESCENCE INTENSITY
404
385
342
428
446
350
400
450
mμ
BENZ (c) acridine


FLUORESCENCE INTENSITY
385
406
407
428
430
450
458
370
420
470
520
mμ
BENZ (a) anthracene

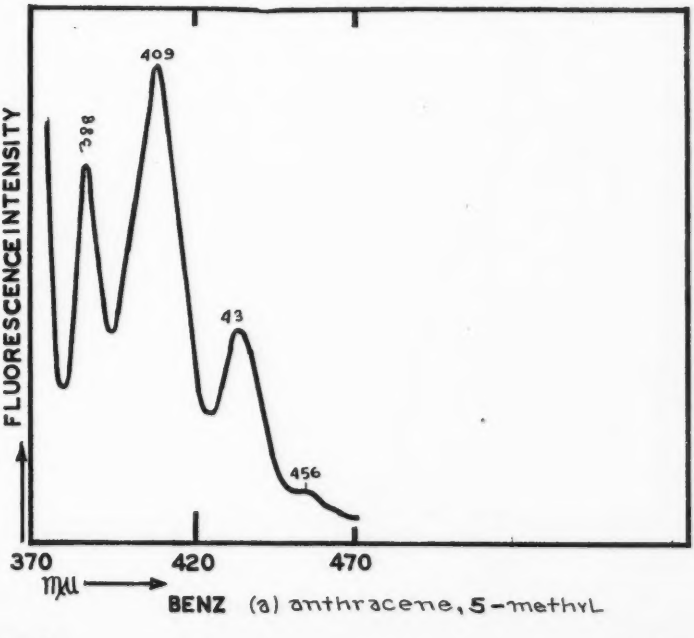

FLUORESCENCE INTENSITY
408
389
432
456
370
420
470
520
mμ
BENZ (a) anthracene, 1-methyl


409
388
434
456
FLUORESCENCEINTENSITY
370
420
470
mμ
BENZ (a) anthracene, 2- methyL

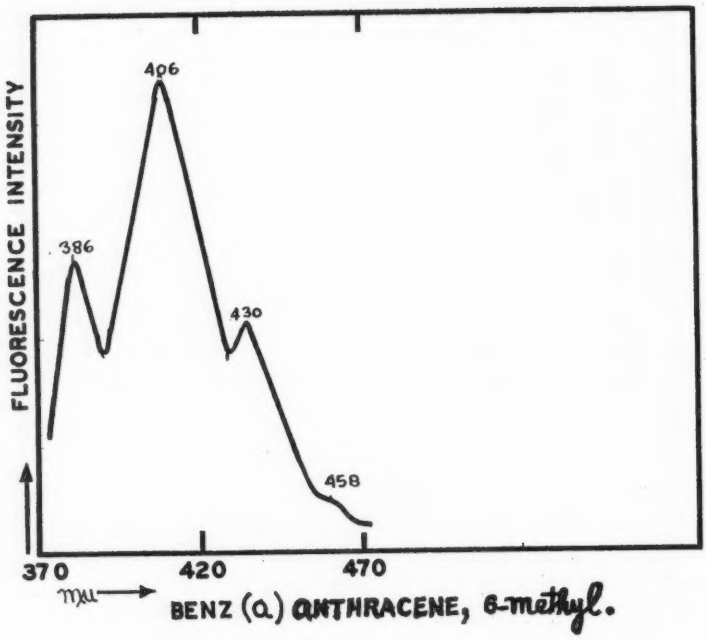

383
406
395
428
450
FLUORESCENCE INTENSITY
370
420
470
mμ
BENZ (a) anthracene, 3-methyL

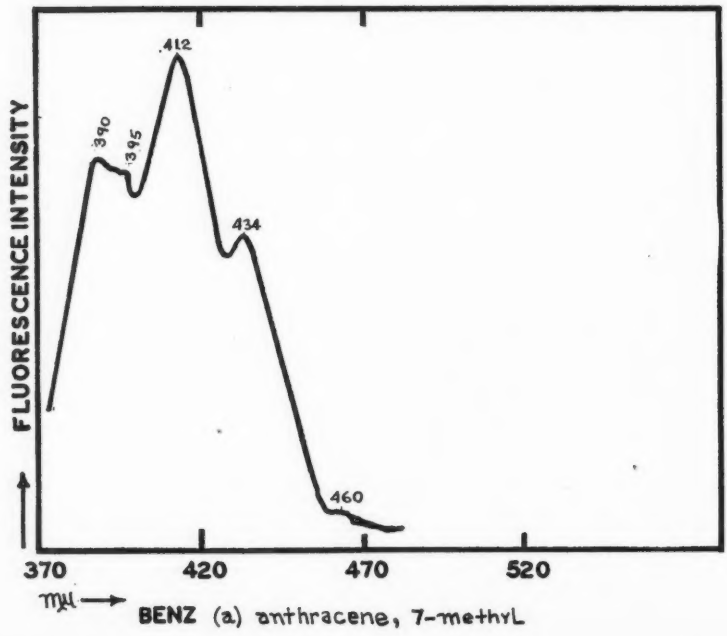


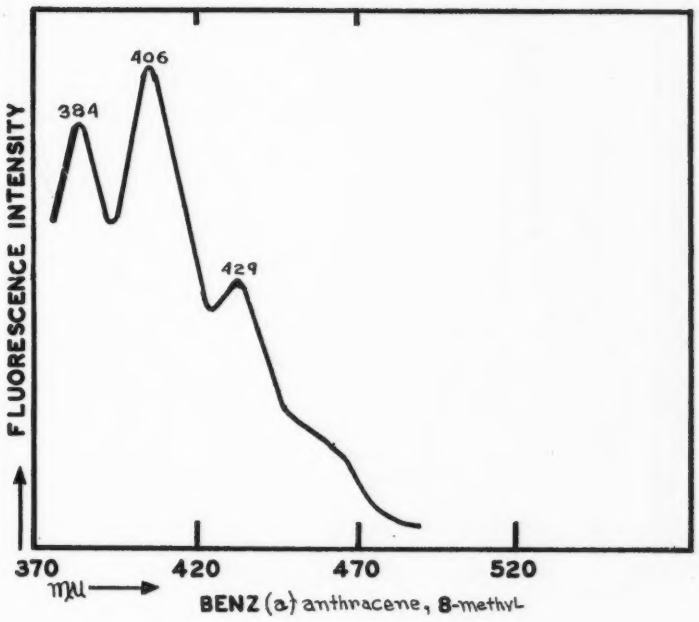
BENZ (a) anthracene, 4-methyL

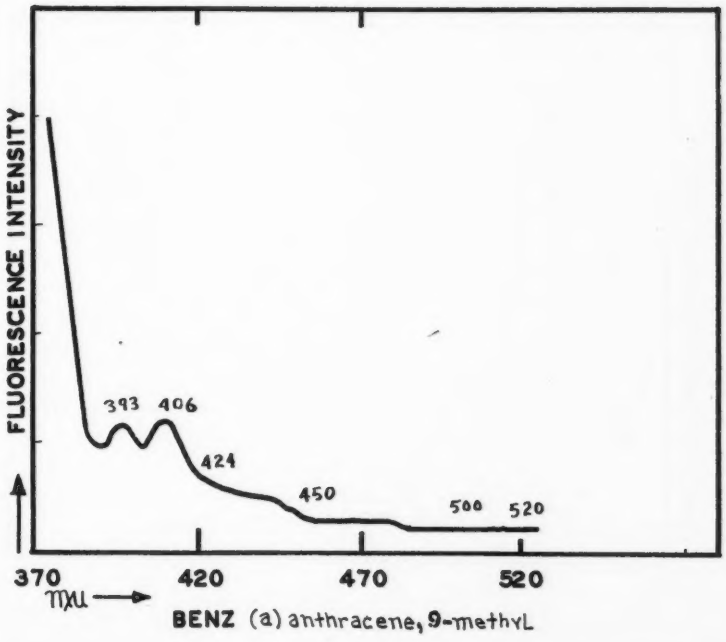


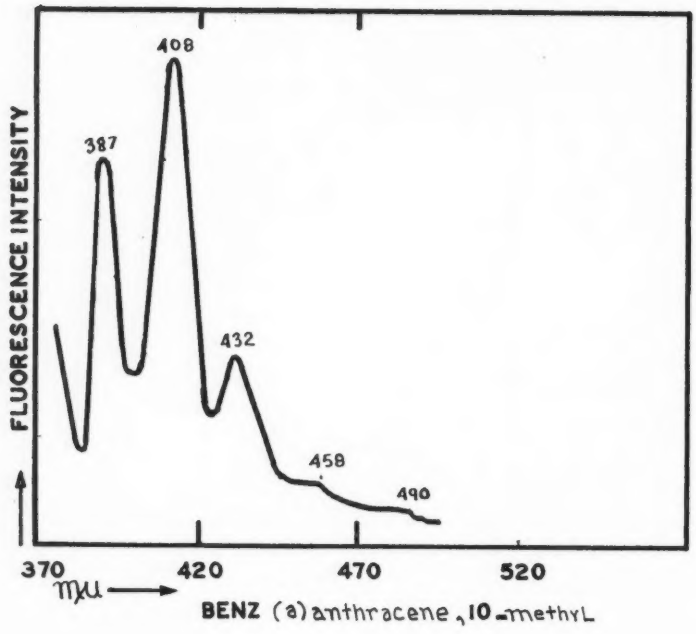
BENZ (a) anthracene, 5-methyL

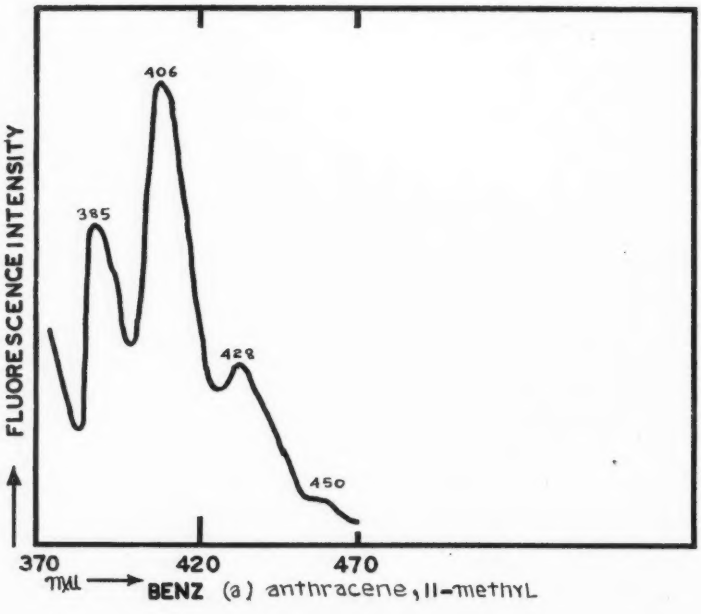

FLUORESCENCE INTENSITY
406
386
430
458
370
420
470
mμ
BENZ (a) ANTHRACENE, 6-methyl.

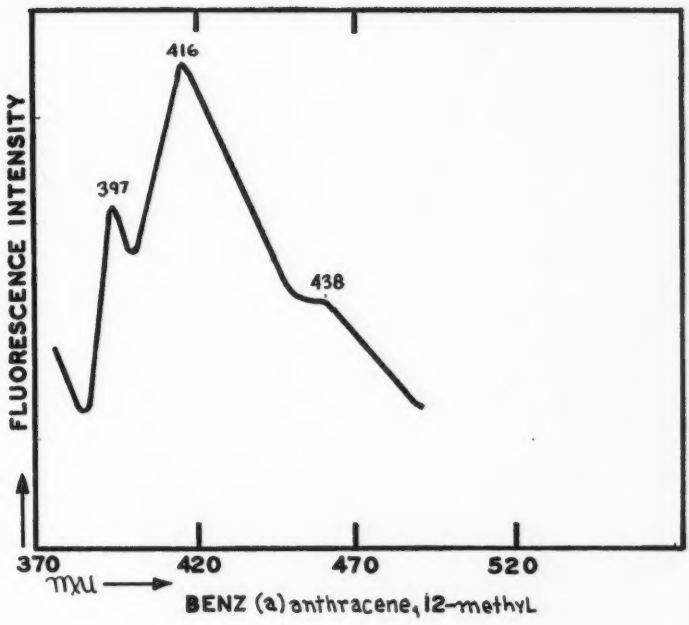

FLUORESCENCE INTENSITY
412
390
395
434
460
370
420
470
520
mμ
BENZ (a) anthracene, 7-methyl

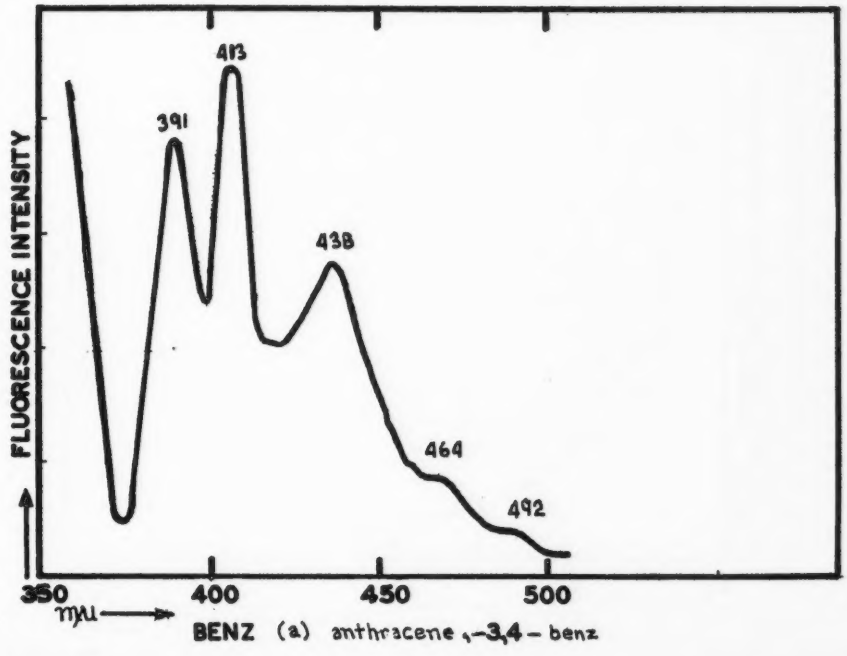

406
384
429
FLUORESCENCE INTENSITY
370
420
470
520
mμ
BENZ (a) anthracene, 8-methyl

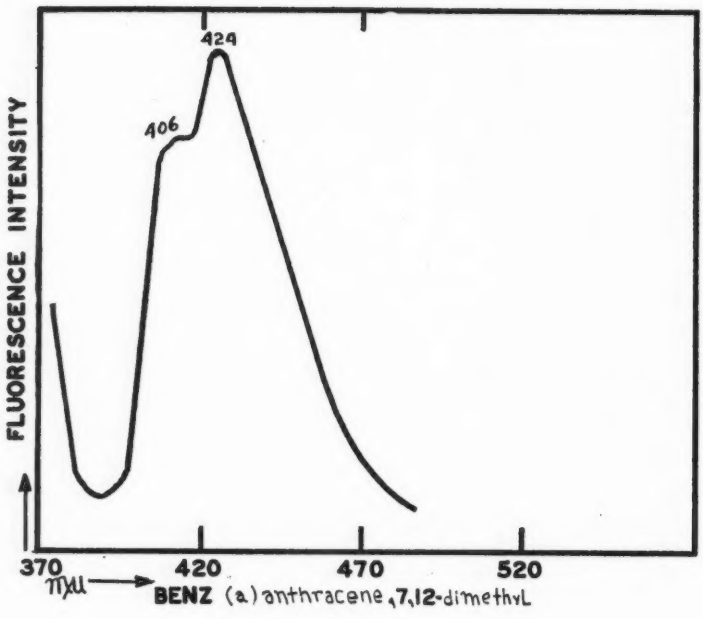

FLUORESCENCE INTENSITY
393
406
424
450
500
520
370
420
470
520
mμ
BENZ (a) anthracene, 9-methyl

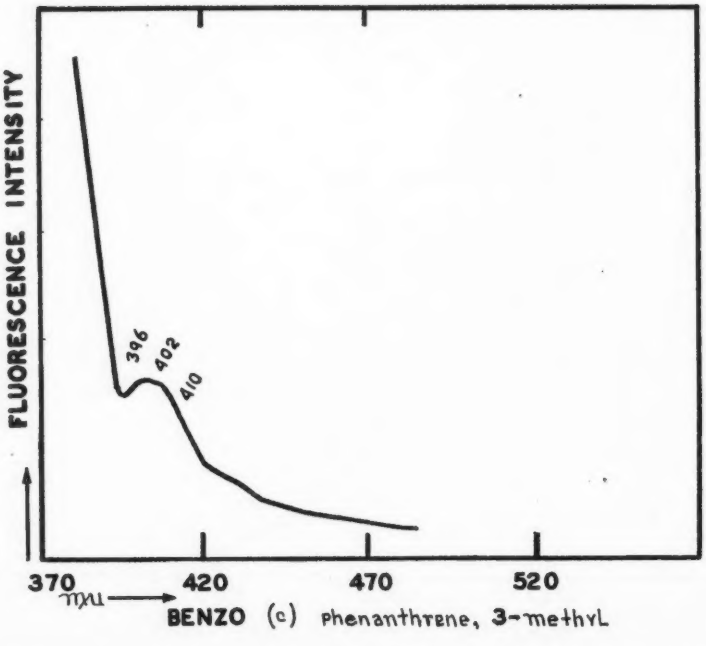

FLUORESCENCE INTENSITY
408
387
432
458
490
370
420
470
520
mμ
BENZ (a) anthracene, 10-methyl

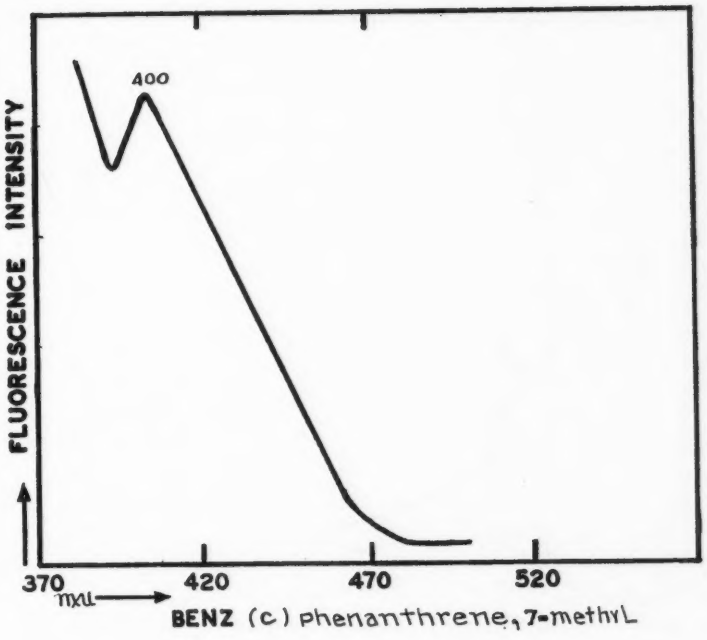

FLUORESCENCE INTENSITY
406
385
428
450
370
420
470
mμ
BENZ (a) anthracene, 11-methyl

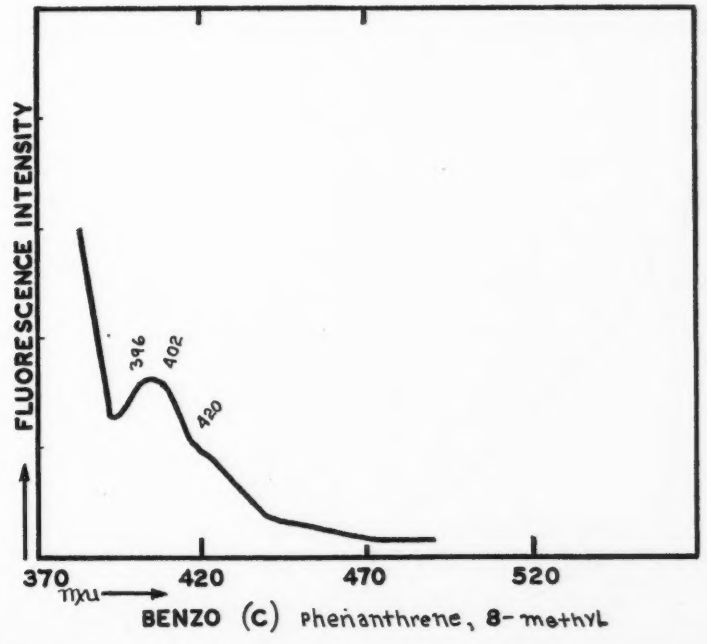

FLUORESCENCE INTENSITY
416
397
438
370
420
470
520
mμ
BENZ (a) anthracene, 12-methyl

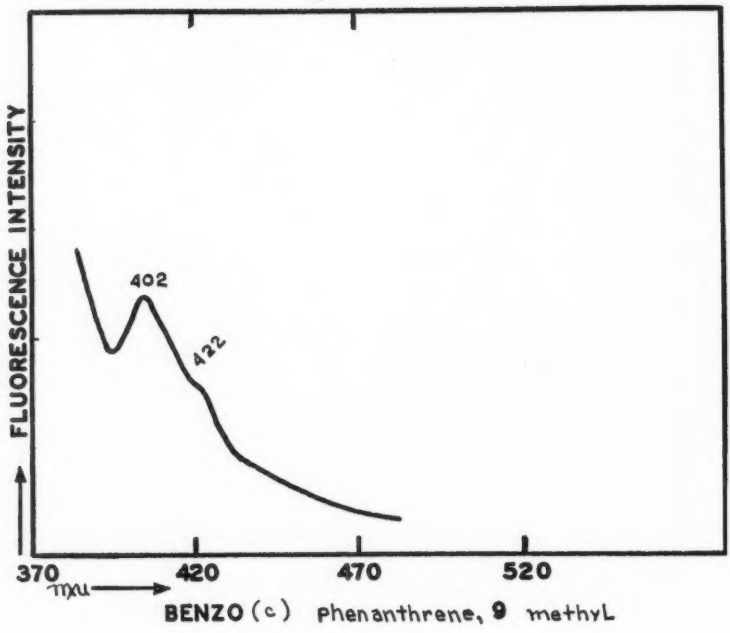

FLUORESCENCE INTENSITY
413
391
438
464
492
350
400
450
500
mμ
BENZ (a) anthracene, -3,4 - benz

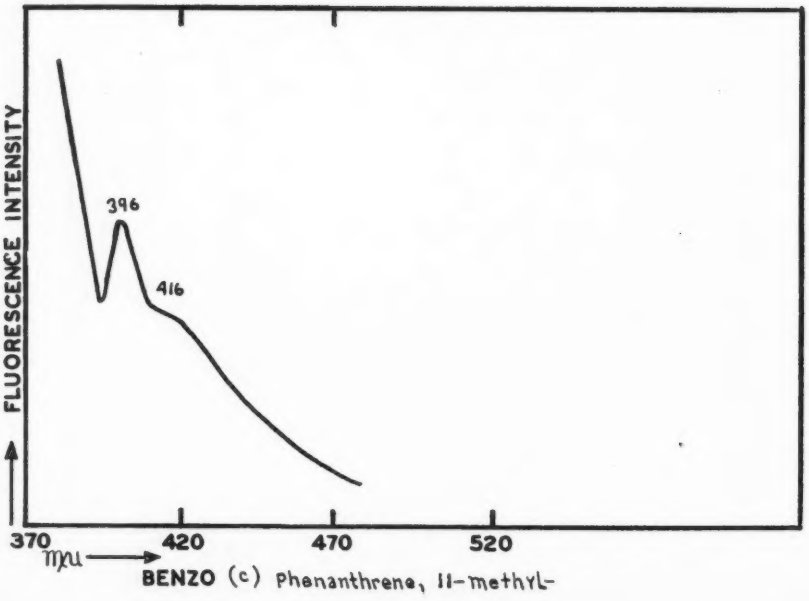

424
406
FLUORESCENCE INTENSITY
370
420
470
520
mμ
BENZ (a) anthracene, 7,12-dimethyl

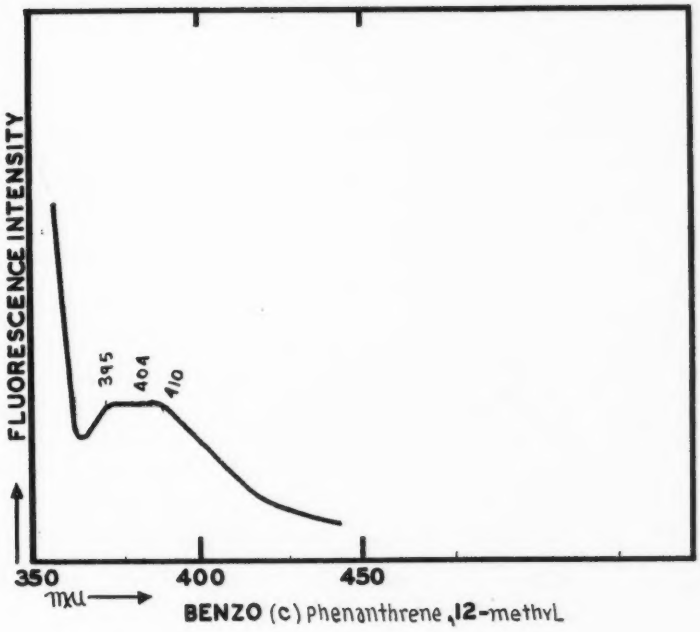

396
402
410
FLUORESCENCE INTENSITY
370
420
470
520
mμ
BENZO (c) phenanthrene, 3-methyl

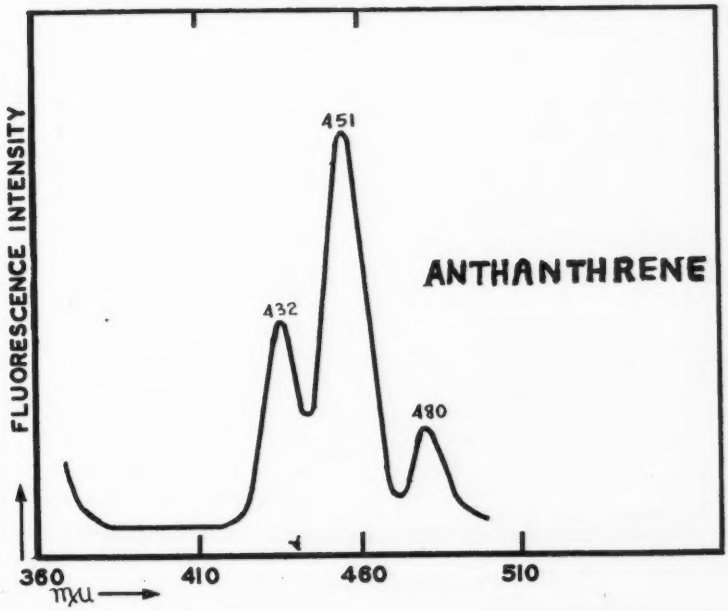

FLUORESCENCE INTENSITY
400
370
420
470
520
mμ
BENZ (c) phenanthrene, 7-methyl

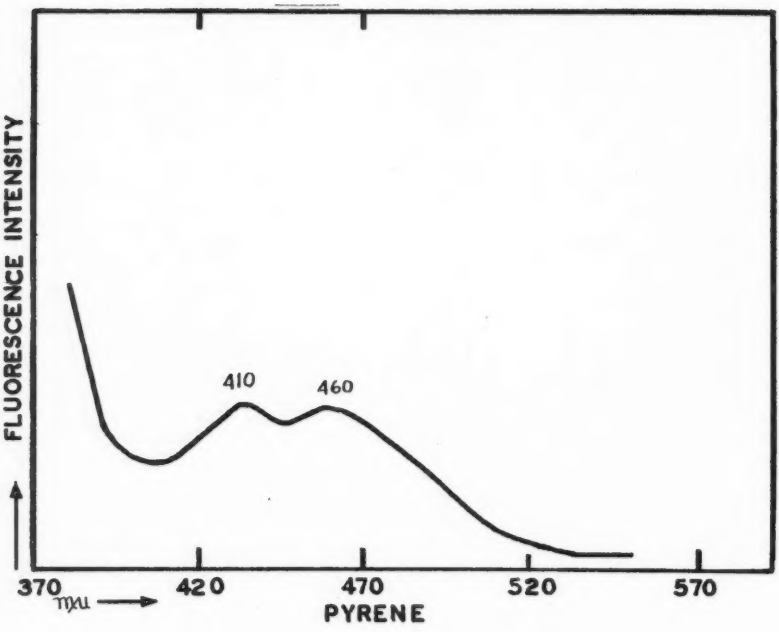

FLUORESCENCE INTENSITY
396
402
420
370
420
470
520
mμ
BENZO (C) phenanthrene, 8-methyl

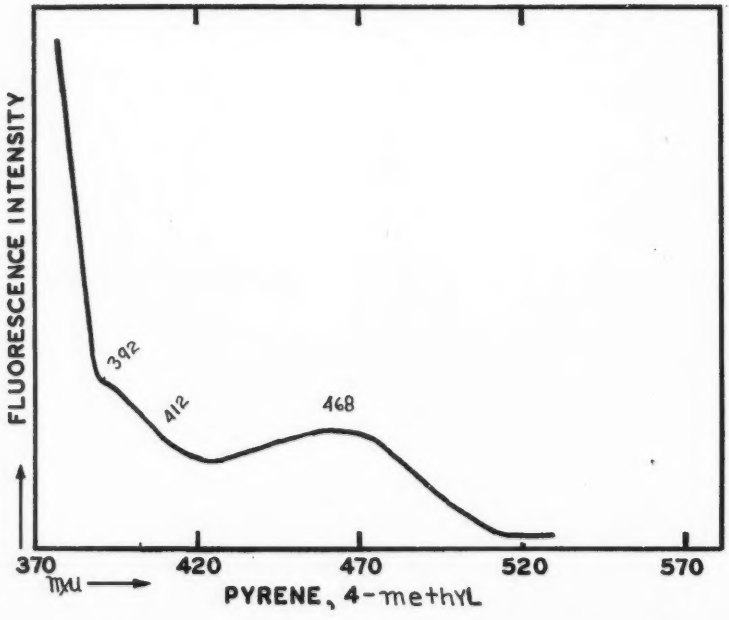

FLUORESCENCE INTENSITY
402
422
370
420
470
520
mμ
BENZO (c) Phenanthrene, 9 methyL

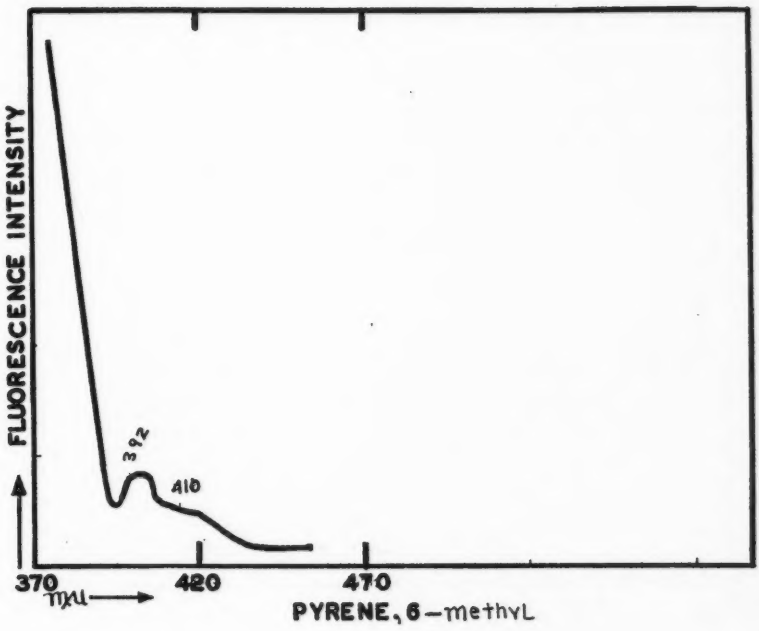

FLUORESCENCE INTENSITY
396
416
370
420
470
520
mμ
BENZO (c) Phenanthrene, 11-methyL-

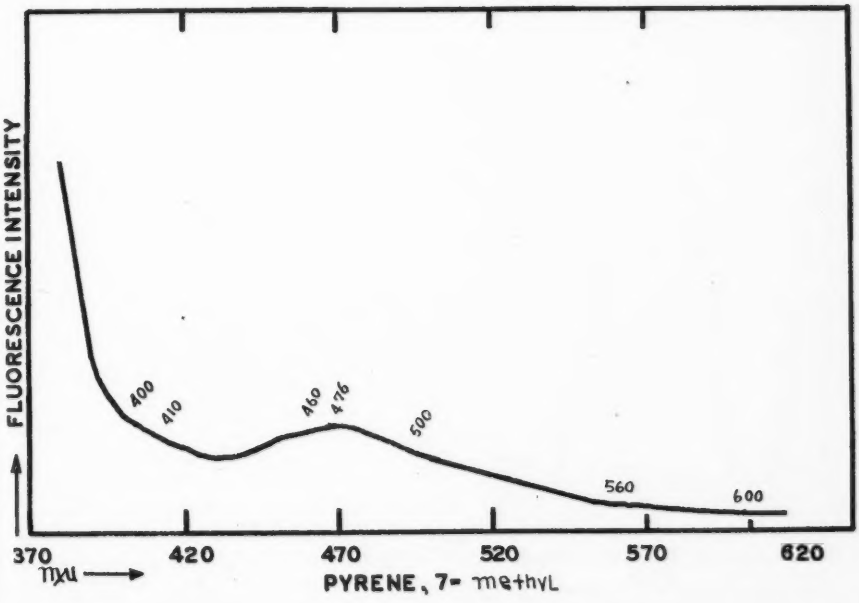

FLUORESCENCE INTENSITY
395
404
410
350
400
450
mμ
BENZO (c) Phenanthrene, 12-methyl

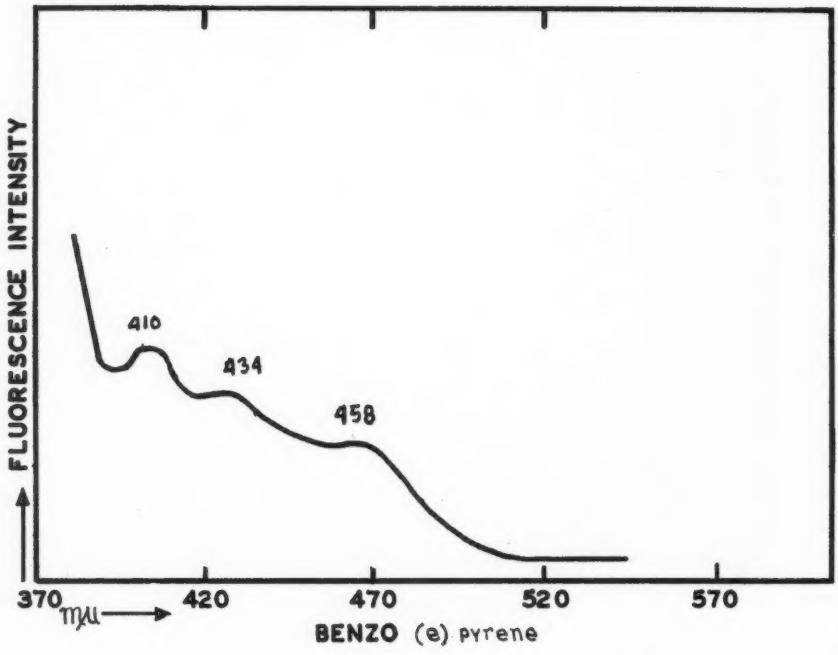

FLUORESCENCE INTENSITY
451
ANTHANTHRENE
432
480
360
410
460
510
mμ

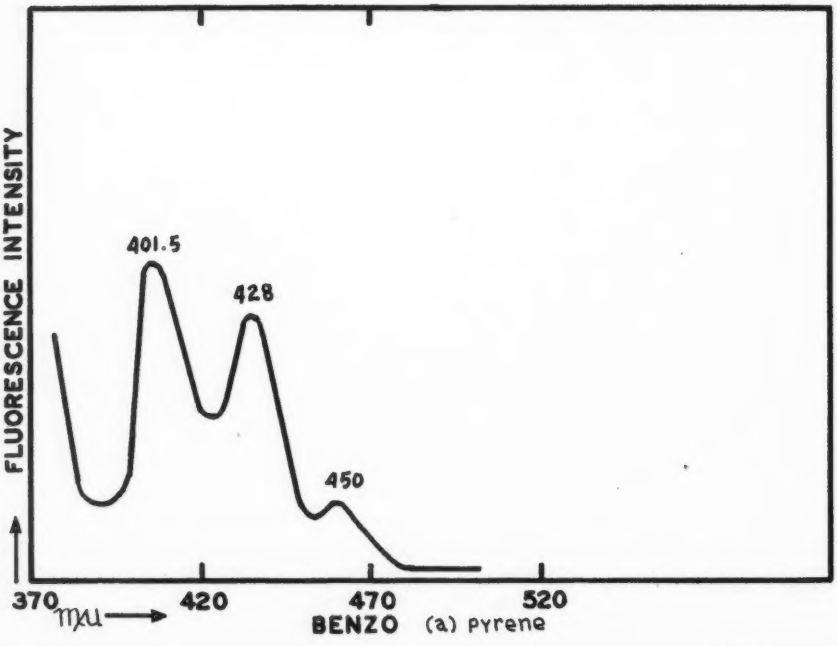

FLUORESCENCE INTENSITY
410
460
370
mμ
420
470
520
570
PYRENE

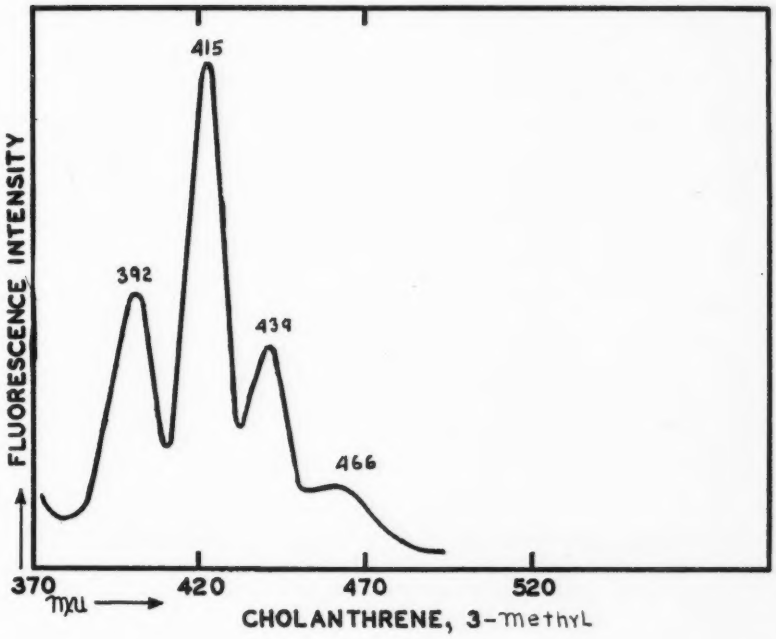

FLUORESCENCE INTENSITY
392
412
468
370
mμ
420
470
520
570
PYRENE, 4-methyl

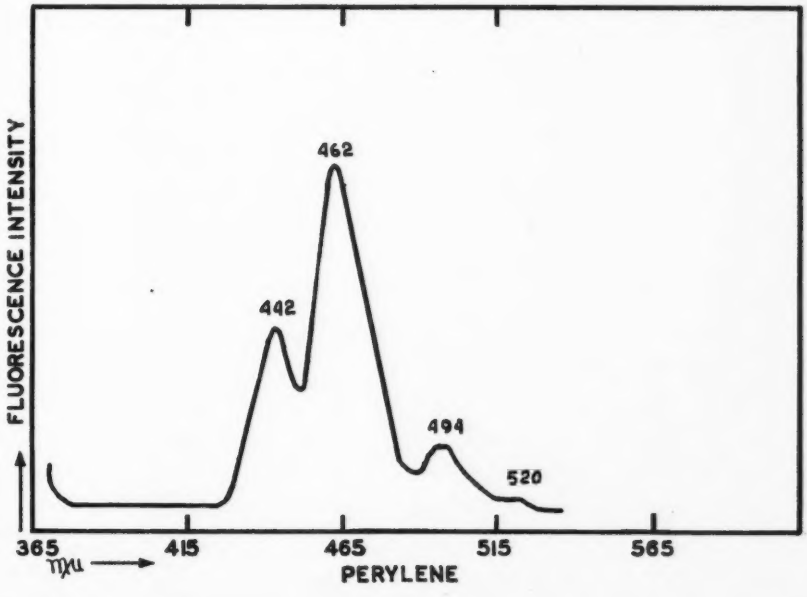

FLUORESCENCE INTENSITY
392
410
370
420
470
mμ
PYRENE, 6-methyl

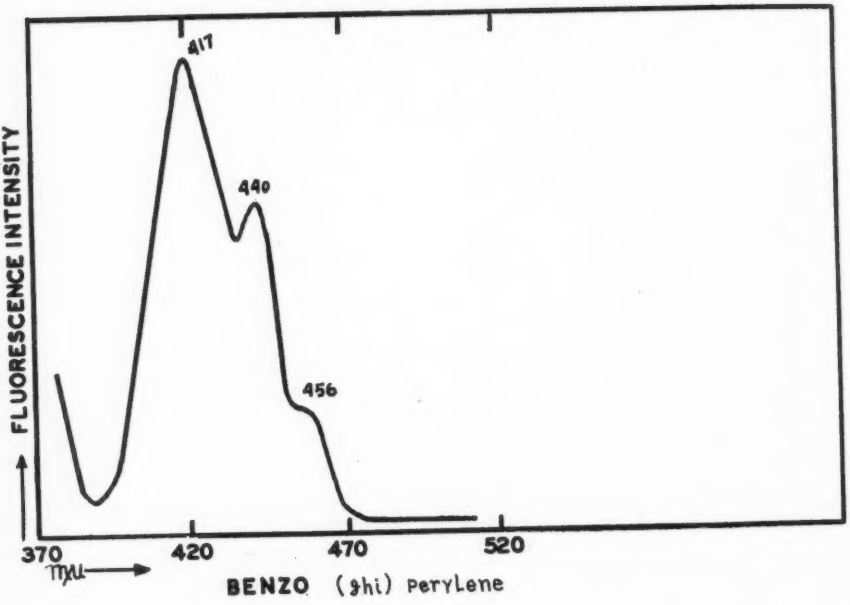

FLUORESCENCE INTENSITY
400
410
460
476
500
560
600
370
420
470
520
570
620
mμ
PYRENE, 7- methyl

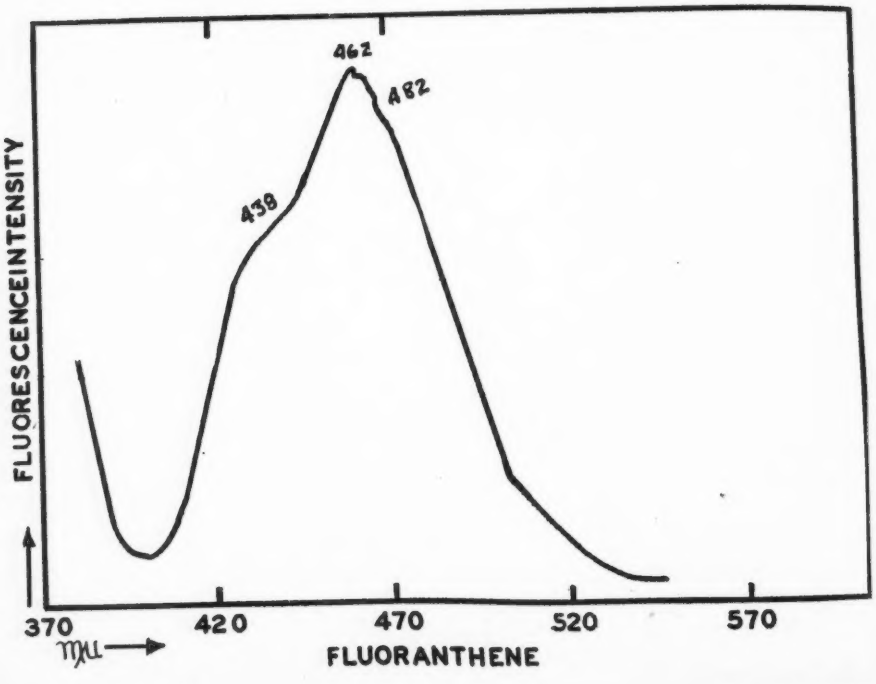

FLUORESCENCE INTENSITY
410
434
458
370
mμ
420
470
520
570
BENZO (e) pyrene

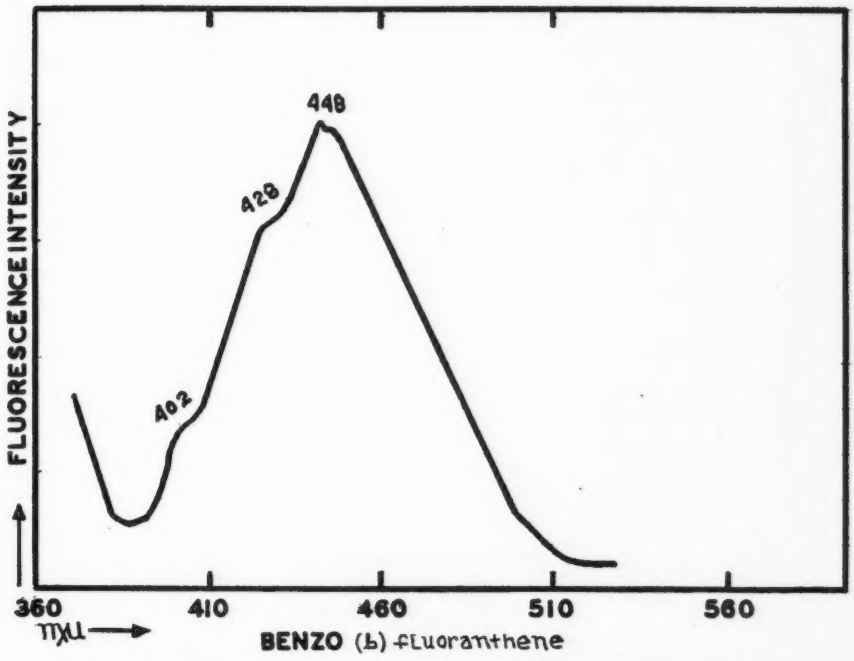

FLUORESCENCE INTENSITY
401.5
428
450
370
mμ
420
470
520
BENZO (a) pyrene

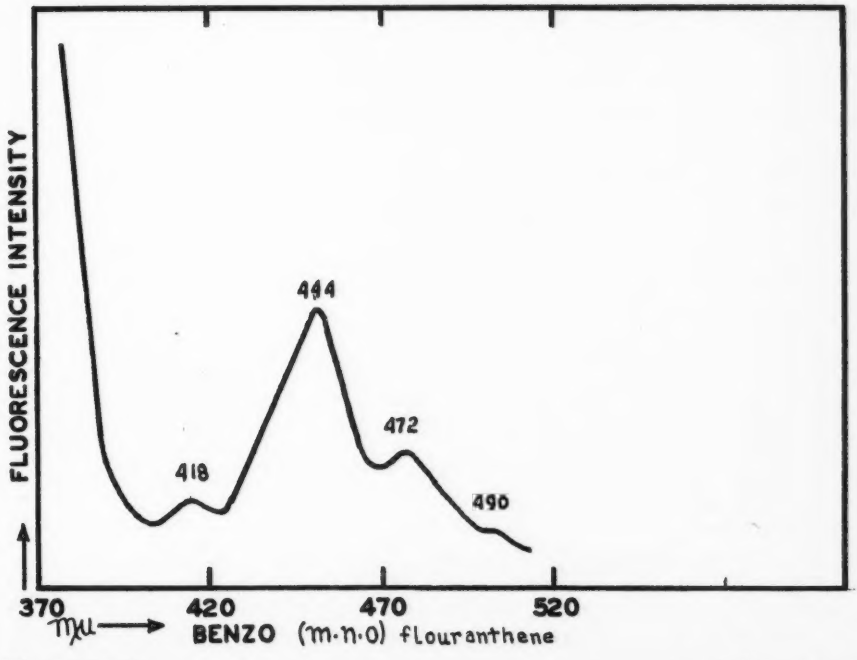

415
392
439
466
FLUORESCENCE INTENSITY
370
420
470
520
mμ
CHOLANTHRENE, 3-Methyl

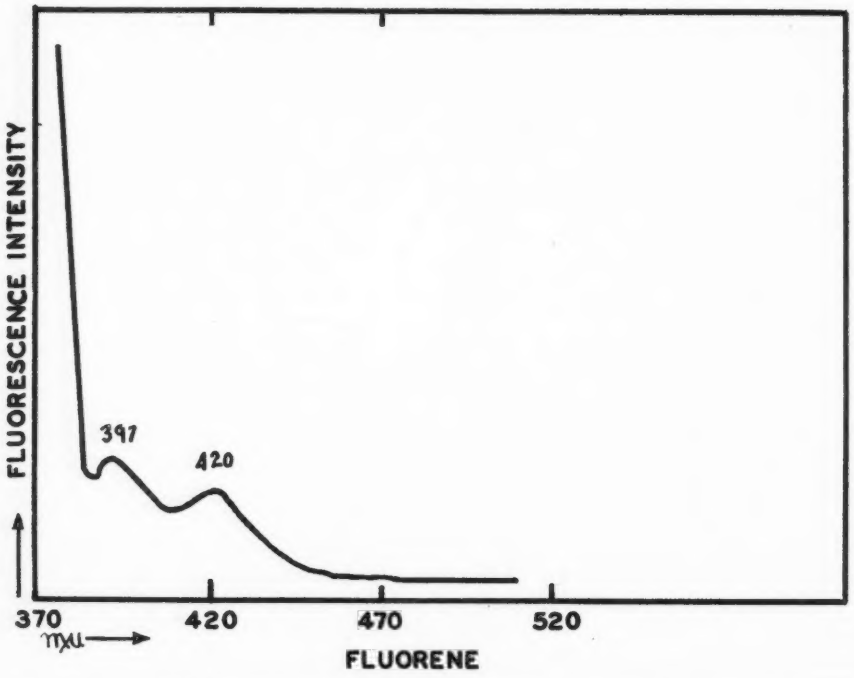

462
442
494
520
FLUORESCENCE INTENSITY
365
415
465
515
565
mμ
PERYLENE

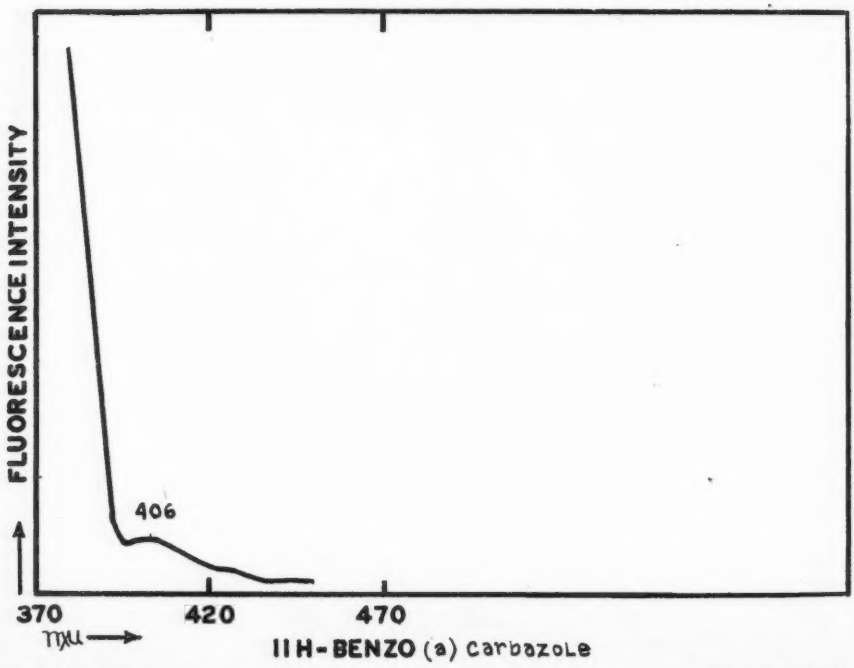

417
440
456
FLUORESCENCE INTENSITY
370
420
470
520
mμ
BENZO (ghi) Perylene

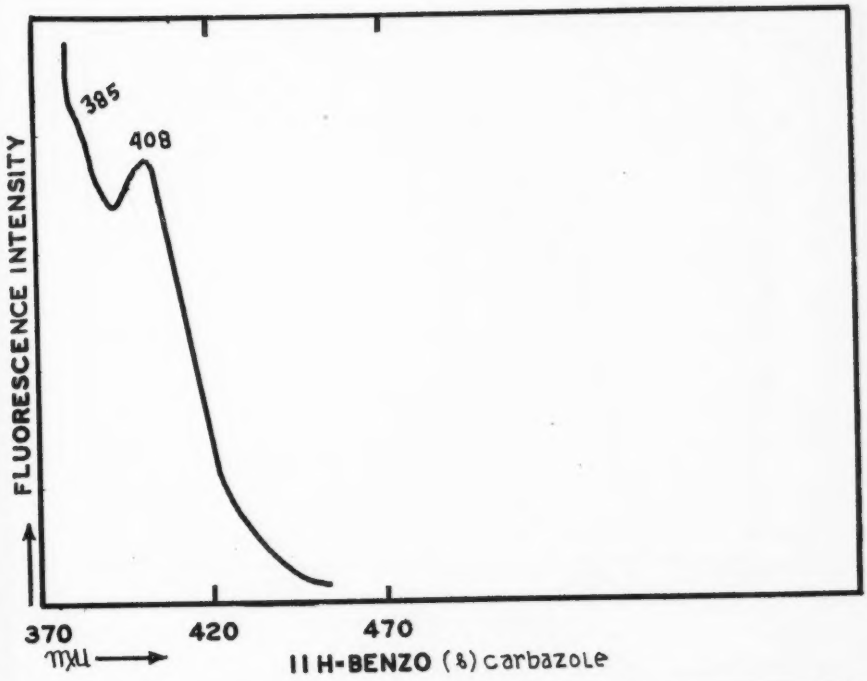

462
482
438
FLUORESCENCEINTENSITY
370
420
470
520
570
mμ
FLUORANTHENE

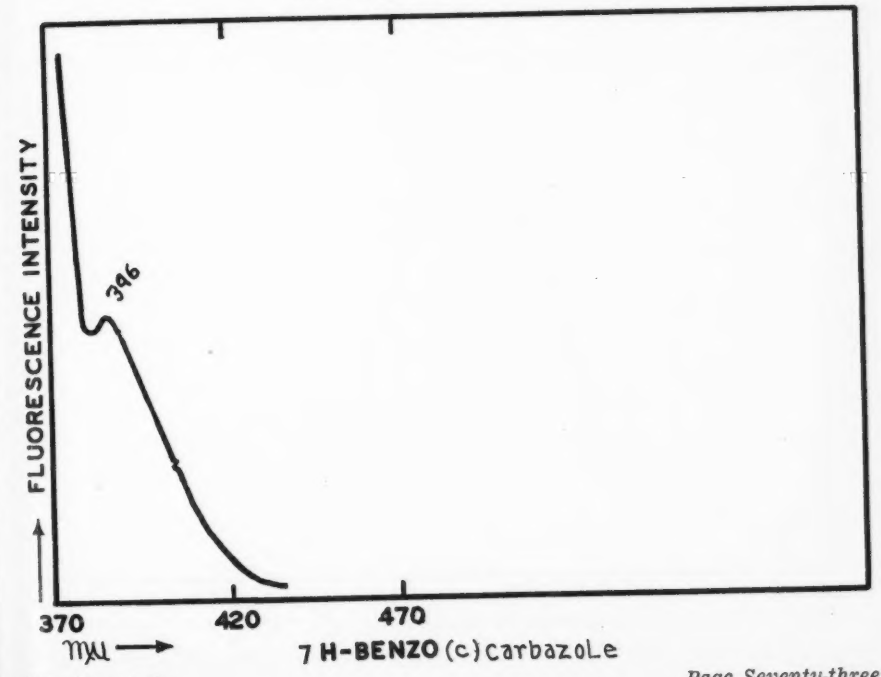

FLUORESCENCE INTENSITY
448
428
402
360
410
460
510
560
mμ
BENZO (b) fluoranthene

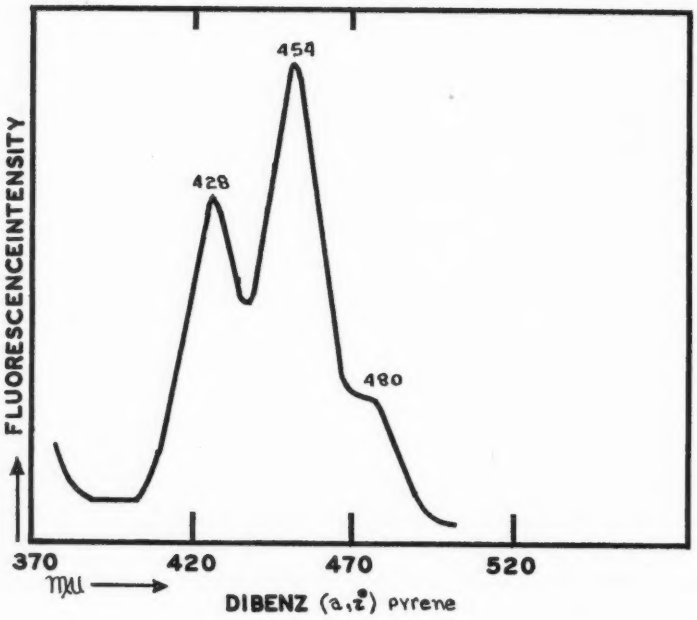

FLUORESCENCE INTENSITY
444
472
418
490
370
420
470
520
mμ
BENZO (m·n·o) flouranthene

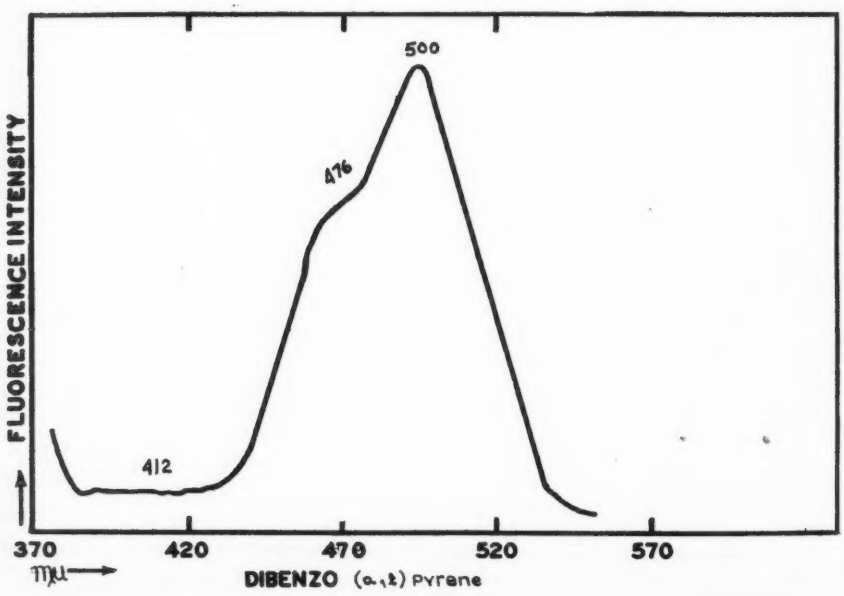

FLUORESCENCE INTENSITY
397
420
370
420
470
520
mμ
FLUORENE

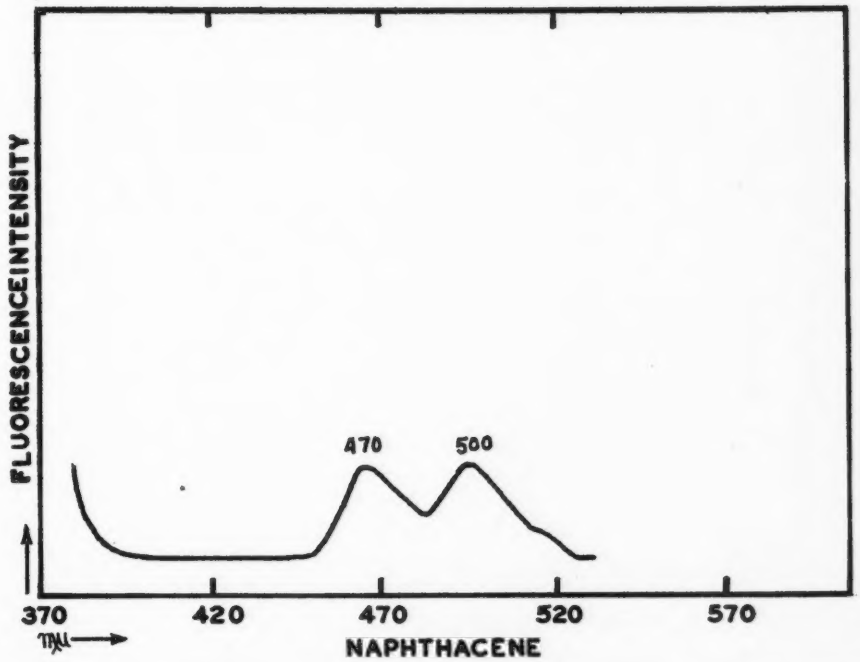

FLUORESCENCE INTENSITY
406
370
420
470
mμ
11H-BENZO (a) Carbazole

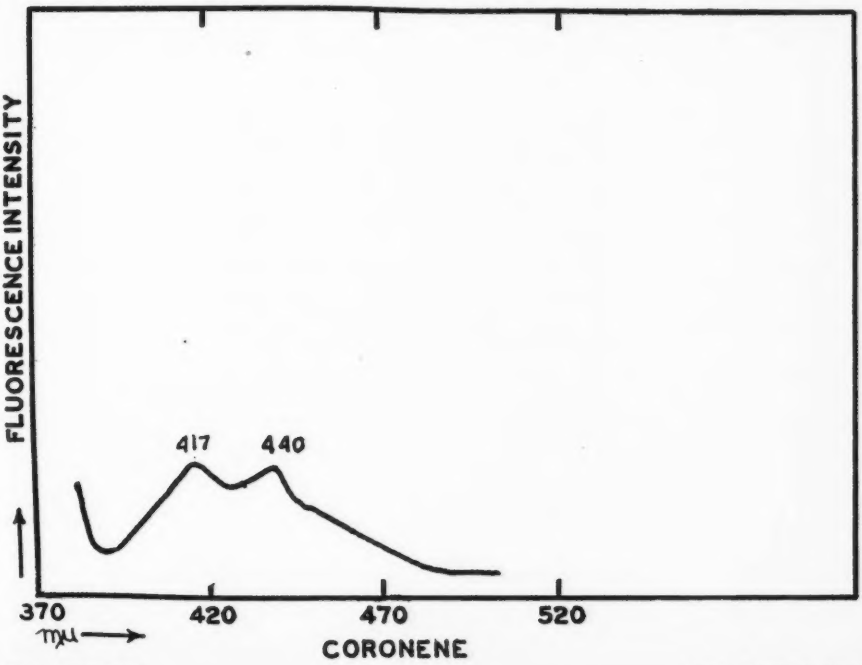

385
408
FLUORESCENCE INTENSITY
370
420
470
mμ
11 H-BENZO (a) carbazole

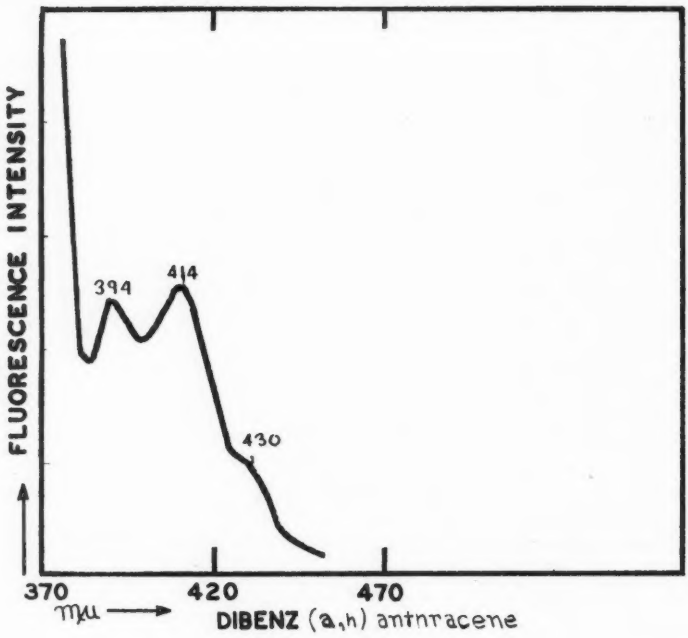

396
FLUORESCENCE INTENSITY
370
420
470
mμ
7 H-BENZO (c) carbazole


454
428
480
FLUORESCENCEINTENSITY
370
420
470
520
mμ
DIBENZ (a,i) pyrene


500
476
412
FLUORESCENCE INTENSITY
370
420
470
520
570
mμ
DIBENZO (a,i) Pyrene


FLUORESCENCEINTENSITY
470
500
370
420
470
520
570
NAPHTHACENE


FLUORESCENCE INTENSITY
417
440
370
420
470
520
CORONENE



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BOOK REVIEWS

EXPERIMENTAL SURGERY (INCLUDING SURGICAL PHYSIOLOGY). J. Markowitz, M.B.E., J. Archibald and H. G. Downil. Fourth edition. The Williams & Wilkins Company, Baltimore, 1959.

This book is a product of the Ontario Veterinary College, Guelph, Ontario. The fourth edition contains many revisions and new chapters added since the first edition was printed in 1937. The new chapters include information on the prostate gland, hypothermia, and the experimental surgery of the Central Nervous System. Likewise, many of the most recent advances in theory and practice are discussed in the sections on vascular surgery and tissue transplantation.

This book is of definite value not only to the surgeon but also to the student, either graduate or undergraduate, who is interested in the subject of surgery and physiology. It serves as a reference book for established principles and also discusses the newer concepts. It shows the value of mammalian experimentation in solving many of the practical problems which arise in the practice of modern day surgery.

Without a doubt this text belongs on the bookshelf of every general surgeon, but will also prove invaluable to the urologist (Experimental Surgery of the Kidney; Experimental Surgery of the Prostate Gland), the orthopedist (Experimental Surgery of the Joints; Experimental Surgery of Bone) and, of course, all those who are interested in experimental biology.

E.M.K.

CLINICAL DERMATOLOGY FOR STUDENTS AND PRACTITIONERS. Harry M. Robinson, Jr., B.S., M.D. and Raymond C. V. Robinson, B.S., M.D., M.Sc. (Med.). The Williams & Wilkins Company, Baltimore, 1959. 242 pages.

In these 242 pages the authors have given concise coverage to the gamut of dermatological disorders and have given emphasis to the fact that dermatologic problems are not only "skin deep." It is brought out that the entire patient must be taken into account and that cursory visual glances will not, on the whole, lead to the diagnosis. Therefore, dermatologic morphology, pathologic diagnosis and diagnostic techniques are well covered in this book.

The book is divided into two parts. The first part deals with general considerations of dermatology, under which are included anatomy, physiology and chemistry of the skin, diagnostic procedures, etc. The second part is devoted to the specific morphology of skin diseases and is augmented by very fine illustrations and charts of differential diagnosis.

This book is designed primarily for students, however it will also appeal to the internist in view of its clear illustrations of specific dermatologic manifestations of systemic diseases.

The only short-coming of this book is its lack of a source of reference material which might direct one toward more detailed information on specific topics. Nonetheless, the authors have successfully written a volume which is easily read and which presents an excellent introduction to the subject.

A.S.W.